

## Masters Research Report



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## **ABSTRACT**

In 2008, 1.8 million children under the age of 15 were living with HIV/AIDS in sub-Saharan Africa. The same report estimates that in 2008, there were 390 000 new infections in children below the age of 15 in Sub-Saharan Africa. Children appear to be the generation most affected by the HIV/AIDS epidemic. With the introduction of Highly Active Antiretroviral therapy (HAART) more perinatally infected children are living into adolescence and beyond. They will have to learn to live with a stigmatising, potentially fatal chronic illness.

Health care workers can no longer rely solely on traditionally used outcome measures, such as viral loads and CD4+ percentages, to monitor effectiveness of interventions and treatments. Quality of Life (QoL) has been suggested as an additional essential outcome measure in clinical practice and research involving children living with a chronic illness. In this research the concept of Health Related Quality of Life (HRQoL) is evaluated in HIV-infected children using the PedsQL 4.0 Generic Core Scale (child self-reports, ages five-seven). The PedsQL 4.0 Generic Core Scales has been found to be a valid and reliable HRQoL measurement tool in children with chronic diseases, school-going children and children infected with HIV.

Domains of Physical, Emotional, Social and School Functioning were evaluated. The children in the comparison group scored significantly higher ( $p<0.01$ ) indicating a better quality of life. The HIV-infected children scored significantly lower in all four domains, with Physical Functioning being most affected ( $p<0.01$ ). The children with HIV were found to be shorter ( $p<0.01$ ) and lighter ( $p<0.01$ ) than those in the comparison group. This could be a contributing factor to the physical difficulties experienced by the HIV-infected children. No relationship could be established between total scores of HRQoL and CD4+ percentages, viral load and duration of HAART treatment.

Demographic data collected indicate that the HIV-infected children were more likely to have a primary caregiver with a lower level of education ( $p=0.01$ ) and more likely to be receiving a Dependency Care Grant ( $p=0.05$ ).

The HRQoL results of this study are similar to those conducted in other parts of the world. The results stress the need for a multi-disciplinary approach when treating HIV-infected children. It has become essential to focus on the medical, physical and psychosocial functioning of the HIV-infected child thereby promoting participation in the family, school and the broader community.


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## DECLARATION

I declare that this research report is my own unaided work, except to the extent indicated in the reference citation and acknowledgements. It is being submitted in partial fulfillment of the requirements for the degree Masters of Science in Medicine (Child Health Neurodevelopment) at the University of the Witwatersrand. It has not been submitted before for any other degree or examination in any other university.

 (B Sc physiotherapy)

Linda Goldberg

....2.nd.....day of .....May.....2011

## **LIST OF ABBREVIATIONS**

AIDS	- Acquired Immune Deficiency Syndrome
HIV	- Human Immunodeficiency Virus
HAART	- Highly Active Antiretroviral Therapy
QoL	- Quality of life
HRQoL	- Health related quality of life
WHO	- World Health Organisation
UNAIDS	- Joint United Nations Programme for HIV/AIDS
FSIQ	- Full Scale Intelligence Quotient

## TABLE OF CONTENTS

	Page
<b>Abstract</b>	ii
<b>Acknowledgement</b>	iv
<b>Declaration</b>	v
<b>List of Abbreviations</b>	vi
<b>Table of Contents</b>	vii
<b>Chapter 1- Introduction</b>	1
<b>Chapter 2 –Literature Review</b>	5
2.1 Introduction	5
2.2 Mother-to- Child Transmission and Diagnosis Of HIV in Young Children	7
2.3 Classification of Paediatric HIV Infection	8
2.4 Highly Active Antiretroviral Therapy	9
2.5 Adherence to HAART in Paediatric Patient	11
2.6 HIV Related Central Nervous System Disease in Children And Associated Motor and Cognitive Development	13
2.7 Growth Patterns in Children with HIV	18
2.8 Psychosocial Well-being and Adjustment of HIV-Infected Children	20
2.9 Psychiatric and Behavioral Disorders Associated With HIV	21
2.10 Disclosure	24
2.11 Coping Mechanisms and Psychosocial Adjustment	27
2.12 Family-Centered Interventions and Psychosocial Adjustment	28
2.13 Socioeconomic Factors Affecting HIV-Infected Children in South Africa	28

2.14	Quality of Life	30
2.15	Quality of Life of Children with Chronic Diseases	32
2.16	Measurement of Health Related Quality of Life	33
2.17	Measurement Tools	34
2.17.1	PedsQL 4.0 Generic Core Scales	34
2.17.2	International Classification of Function, Disability and Health	36
2.17.3	Household Economic and Social Status Inventory	37
2.18	Health Related Quality of Life of Children infected with HIV	37
2.19	Conclusion	40
<b>Chapter 3- Methods</b>		<b>41</b>
3.1	Location of Study	41
3.2	Ethical Clearance	41
3.3	Study Population	41
3.4	Sample Selection	42
3.4.1	Study Group	42
3.4.2	Comparison group	43
3.5	Assessment Tools	44
3.6	Procedure	44
3.6.1	Translation of PedsQL 4.0 Generic Core Scales	44
3.6.2	Study Group	45
3.6.3	Comparison group	46
3.7	Sample Size	47
3.8	Statistical Analysis	47
<b>Chapter 4- Results</b>		<b>48</b>
4.1	Demographics	48
4.1.1	Gender Distribution	48
4.1.2	Age Distribution	48
4.1.3	Comparison group Composition	49
4.2	Socioeconomic Environment	49
4.2.1	Caregiver Relationship and Distribution	50



4.2.2	Caregiver Educational Level	50
4.2.3	Employment Status of Caregiver and Care Dependency Grants	51
4.2.4	Housing	52
4.3	Anthropometric Analysis (height, weight and BMI)	53
4.4	Analysis of PedsQL 4.0 Generic Core Scale Scores	53
4.5	Analysis of HRQoL Scores, Duration of HAART Therapy CD4+ and Viral Loads	55
4.6	Summary of Findings	55
<b>Chapter 5 – Discussion</b>		<b>57</b>
5.1	Demographics	57
5.2	Comparison group	59
5.3	PedsQL 4.0 Generic Core Scale	59
5.4	Limitations of Research	63
5.5	Relevance to Clinical Practice and Recommendations Based on the Results	64
5.6	Recommendations for Future Research	64
<b>Chapter 6 - Conclusion</b>		<b>66</b>
<b>Chapter 7- References</b>		<b>68</b>
<b>Appendix I</b>	PedsQL 4.0 Generic Core Scale	89
<b>Appendix II</b>	Scoring of PedsQL 4.0 Generic Core Scale	90
<b>Appendix III</b>	HESSI Questionnaire	91
<b>Appendix IV</b>	Ethical Clearance Certificates	93
<b>Appendix V</b>	Consent Forms	94
<b>Appendix VI</b>	Zulu translation of PedsQL 4.0 Generic Core Scale, Child Self-Report (Ages 5-7)	105

## **List of Tables**

<b>Table 4.1</b>	<b>Gender Distribution</b>	<b>48</b>
<b>Table 4.2</b>	<b>Age Distribution</b>	<b>49</b>
<b>Table 4.3</b>	<b>Educational Level of Primary Caregiver</b>	<b>51</b>
<b>Table 4.4</b>	<b>Employment Status of Primary Caregiver And Care Dependency Grant</b>	<b>52</b>
<b>Table 4.5</b>	<b>Growth Parameters</b>	<b>53</b>
<b>Table 4.6</b>	<b>Analysis of PedsQL 4.0 Generic Core Scale</b>	<b>54</b>

## **List of Figures**

<b>Figure 4.1</b>	<b>Comparison group Composition</b>	<b>49</b>
<b>Figure 4.2</b>	<b>Caregiver Relationship and Distribution</b>	<b>50</b>
<b>Figure 4.3</b>	<b>Type of Housing</b>	<b>52</b>

## **Chapter 1: INTRODUCTION**

According to the 2009 UNAIDS Report, in Sub- Sahara Region, 1.8 million children under the age of 15 were living with HIV/AIDS in 2008. The same report estimates that in 2008, there were 390 000 new infections in children below the age of 15 in Sub- Saharan Africa (UNAIDS, 2009). By 2010, it has been predicted that 15.7 million children in sub- Sahara Africa (SSA) would have lost at least one parent (Chandan and Richter, 2009). In sub-Saharan Africa, children appear to be the generation most affected by the HIV/AIDS epidemic (Earls et al, 2009). The United Nations Convention on Children's Rights (United Nations, 1998) states that each child has the right to a standard of health and living that would maximise his/her physical, mental, spiritual and social potential. With the introduction of Highly Active Antiretroviral therapy (HAART) more perinatally infected children are living into adolescence and beyond (UNAIDS/WHO, 2006). They will have to learn to live with a stigmatising, potentially fatal chronic illness (Mellins et al 2002).

HIV/AIDS, in the child population, has been associated with developmental delay, growth disturbances, cognitive and psychological problems (Richter, 2004). Since the introduction of HAART, the incidence of severe HIV encephalopathy has decreased (Patel et al, 2009; Mitchell, 2006) however HAART has not been as effective in reducing the more subtle forms of encephalopathy (Mitchell, 2006). Despite HAART, children have been shown to display developmental delay and cognitive impairment (Smith, 2008; Mitchell, 2006). In sub- Saharan Africa despite only 15% of children requiring ARV therapy being treated (UNAIDS 2007), many children are living into adolescence.

An increased rate of psychiatric problems has been associated with children suffering from any chronic condition (Scharko, 2006). Anxiety, depression and attention deficit hyperactivity disorder (ADHD) have all been shown to be common amongst children with HIV/AIDS (Scharko, 2006).

As HIV/AIDS is now considered to be a chronic condition and children have access to more effective clinical interventions and longer life expectancy, we can no longer rely solely on traditionally used outcome measures, such as viral loads and CD4+ percentages, to monitor effectiveness of interventions and of treatments (Garvie et al, 2009; Lee et al, 2006; Missmer et al, 2000). An additional health measure, Quality of Life (QoL), has been suggested to evaluate outcomes for children with chronic health conditions (Lee et al, 2006; Missmer et al, 2000; Wallender and Varni, 1998).

Quality of Life (QoL) has been defined by the WHO as “the individual’s perception of their position in life in the context of culture and value systems in which they live, and in relation to their goals, expectations, standards, and concerns.” (WHOQOL, 1997. Page1). According to Wallender et al (2001) the concept of HRQoL is a narrower approach, as it looks at QoL purely in the medical context, however overall QoL incorporates influences on school, family, friends and other living circumstances. It appears in the literature that the terms HRQoL and QoL are terms that are often used interchangeably (Eiser and Morse, 2001; Wallender and Varni, 1998) and no consensus has been found on the use of the two terms (De Civita et al, 2005).

Research into HRQoL and HIV has focused more on the adult population (Garvie et al, 2009). Despite the limited research, it is becoming evident that HIV/AIDS has a negative impact on the QoL of paediatric patients with HIV (Banerjee et al, 2010; Bomba et al, 2010; Xu et al, 2010; Oberdorfer et al, 2008; Lee et al, 2006; Storm et al, 2005). Some of the factors that may affect health-related quality of life (HRQoL) of children living with HIV/AIDS include – stigma associated with the disease, altered family dynamics, poor access to medical care, poor nutrition, and medication with toxic side effects and (Missmer et al, 2000).

The majority of tools that have been used to assess QoL in patients with HIV/AIDS have focused on adults rather than the paediatric community (Clayson et al, 2006; Berzon and Lenderking, 1998; Shumaker, 1997; Hays and Shapiro, 1992). In a review by Clayson et al (2006), 17 generic and 17 HIV specific tools were assessed. He was however unable to recommend any one of the tools as being the most effective excluding measures due to their extensive length, lack of normative data, insufficient content to comprehensively assess HRQoL and excessive administration. Excessive administration was not qualified in the report.

The PedsQL 4.0 Generic Core Scales (Paediatric Quality of Life Inventory) is a brief, standardised generic assessment instrument that systematically assesses patients' and parents' perceptions of HRQoL in paediatric patients with chronic health conditions (Varni et al, 1999). The measurement tool is designed to measure the core health dimensions delineated by the WHO namely- physical functioning (eight items), emotional functioning (five items), social (five items) and school functioning (five items) (Varni et al, 2001). The PedsQL 4.0 Generic Core Scales are comprised of parallel child self-report for ages five-18 and parent proxy- report for ages two -18. (Varni et al, 2006). The necessity of using child self-reporting in measuring QoL has been stressed in the literature (Rosenbaum, 2008; Eiser and Morse, 2001). The PedsQL4.0 Generic Core Scales have been used in research to assess the health- related quality of life of HIV infected children (Banerjee et al, 2010; Bomba et al, 2010; Xu et al, 2010).

### **Problem statement**

Since the introduction of HAART in South Africa in 2004, the life expectancy of children infected with HIV has increased. It is however important to be able to assess whether this increase in life expectancy is accompanied by a decrease in the quality of life of these children. There are many additional factors, in the South African context, which may affect the quality of life of children in addition to HIV/AIDS.

### **Significance of study**

A search of the literature has shown that there has been very limited research on the HRQoL of children infected with HIV/AIDS in South Africa. The information gathered on the quality of life of children with HIV/AIDS would be of benefit to all the health team members, and family, involved in the treatment of young children with HIV/AIDS. The information would assist in determining the resource allocation that is necessary in terms of social, emotional and school support that would optimise the quality of life of the children with HIV/AIDS. In addition, the specific domains assessed using the PedsQL 4.0 Generic Core Scales may highlight specific aspects of quality of life that are consistently affected by the disease process that need specific intervention and considerations when treating a child with HIV/AIDS holistically.

### **Aims of the study**

- To assess and evaluate the quality of life of children infected with HIV using the PedsQL 4.0 Generic Core Scales

### **Objectives of the study**

- To determine if any specific domain/s assessed in the Generic PedsQL 4.0 Core Scale is more affected in children with HIV/AIDS.
- To determine if there is a relationship between socio-economic factors and quality of life using the HESSI Questionnaire
- To determine if there is a correlation between health status (CD4 count, viral load and antiretroviral therapy) and quality of life
- To compare quality of life of children with HIV/AIDS, using the PedsQL 4.0 Generic Core Scale, to children uninfected with HIV/AIDS.

## **Chapter 2: LITERATURE REVIEW**

With the introduction of highly active antiretroviral therapy (HAART) in the mid 1990s, the life expectancy of children with HIV/AIDS has increased, thus HIV can now be considered as a chronic medical condition (Garvie et al, 2009; Lee et al 2006; Missmer et al, 2000). It has therefore become increasingly important to study the quality of life of children living with HIV/AIDS (Garvie et al, 2009). Using quality of life as a research outcome, we are able to assess the effectiveness of treatments and services on the paediatric population (Missmer et al, 2000).

This literature review serves to discuss the concepts of quality of life (QoL) and health related quality of life (HRQoL) as well as the factors that impact on the quality of life of children living with HIV/AIDS. Key concepts to be discussed include vertical transmission of HIV, classification of disease stages, specific applicable manifestations of HIV in the paediatric and school- aged population, psychosocial adjustment and the psychosocial effects of HIV/AIDS. Articles were found searching Pubmed, Medline and Psychiatry online. A hand search was conducted in the Health Sciences Library at the University of the Witwatersrand.

### **2.1 Introduction**

In Africa, both HIV-1 and HIV-2 have been identified. HIV-2 is found mainly in western African countries and appears to be less virulent than HIV-1 (Zeichner, 2006). For the purposes of this research, HIV-1, found in South Africa, will be referred to as HIV.

In November 2003 the South African government introduced the Comprehensive HIV and AIDS Care, Management and Treatment Plan (South African Government Task Team, 2003), with the national roll-out of HAART beginning in March 2004 (Meyers et al, 2007). As a result the number of children receiving

highly active antiretroviral therapy (HAART) has increased from less than 3000 in 2005 to more than 21 000 in September 2006 (Meyers et al, 2007). However by the end of 2008, the World Health Organisation estimated that there were 94 000 children living in South Africa that required HAART (WHO Progress report, 2009). With the introduction of HAART we have seen a decrease in mortality and morbidity rate in children living with HIV/AIDS (Patel et al 2009; Lee, 2006; Gortmaker et al, 2001). Challenges facing HIV-infected children and their health care providers, at present and in the future, will include associated disabilities, adherence to HAART, disclosure and changing life circumstances (Brown et al, 2010; Lee et al, 2006)

The concept of a chronic childhood disease requires defining so as to ascertain the applicability of the term with reference to HIV/AIDS. Mokkink et al, (2008), defined a childhood chronic disease using four criteria namely: (1) child must be aged younger than 18; (2) the diagnosis is made using scientific knowledge and is reproducible using valid methods and instruments; (3) the disease is considered not curable at time of diagnosis; (4) the condition has been present for more than three months or expected to be so. The above definition reflects only on the medical aspects of a condition without looking at the broader impact a disease might have on a child. This was included in a definition by Perrin et al (1993) who looked at the level of functional impairment associated with a disease or condition and the amount of medical care required ( more than expected for a child of a certain age) . From the above two definitions it is valid to say that HIV/AIDS can be considered a chronic childhood condition/disease.

In the following paragraphs, mother-to child transmission, classification of HIV, HAART, adherence, and growth patterns associated with HIV will be discussed. These topics have been chosen for their relevance to the research.



## **2.2 Mother- to Child Transmission and Diagnosis of HIV in Young Children**

In South Africa women of child-bearing age (15-29) have the highest rates of HIV infection (Karim et al, 2008). More than 90% of paediatric infection is through vertical transmission (WHO Progress Report, 2009; Lourie et al, 2005). It has been suggested that mother-to child transmission (MTCT) can occur in utero, intra-partum (80%), and through breastfeeding (Sturt et al, 2010; Read, 2005). There are various risk factors that have been identified as increasing the risk of MTCT. These include increased mother's viral load, increased duration of exposure especially with ruptured membranes, breastfeeding, mixed breastfeeding and maternal vitamin A deficiency (Read, 2005). Vertical transmission rates, without preventative intervention, have been shown to be between 25-48% in resource-poor, breastfeeding populations and 14-23% in industrialised, non- breastfeeding populations (Gray and McIntyre, 2007; De Cock, 2000). A transmission rate as low as two percent has also been reported in developed countries. This is with the intervention of antiretroviral therapy, caesarean sections and formula feeding. However in most highly affected countries, preventative measures have only managed a 15 percent reduction in transmission (Gray and McIntyre, 2007). In sub- Saharan Africa, where over 85% of all HIV-infected women are found, only 11% have access to preventative mother-to child transmission interventions (UNAIDS/UNICEF 2007). Since the introduction of MTCT intervention measures in South Africa, we are still unable to assess the efficacy of the programmes or the extent of the efficacy (Meyers et al, 2007).

The clinical diagnosis of HIV infection in children older than 18 months is confirmed with two positive rapid tests. If one of the rapid tests is negative, a confirmatory enzyme-linked immunosorbent assay (ELISA) test is indicated. In children younger than 18 months a positive HIV DNA polymerase chain reaction test (PCR) together with a confirmatory viral detection assay is required to positively diagnose HIV. The baseline viral load would have to be above 10 000

copies/mL (National Department of Health, 2010) . With HIV infection both the cell mediated and humoral immune functions of the child are compromised.

According to McFarland (2005), the defining characteristic of HIV, if left untreated, is the continuous reduction of absolute numbers and percentage of CD4+ T lymphocytes of the total lymphocyte count. The risk of opportunistic infections is indirectly proportional to the amount of CD4+ T lymphocytes present in the child's system (McFarland, 2005). According to Coovadia and Wittenberg (2007), the measure of the viral load (HIV-RNA copy number) in the infant is of importance as it offers us a prognostic value i.e. the higher the viral load the more rapid the disease progression. However McFarland (2005) states that CD4+ percentage is a more reliable indicator of disease progression. There is an inverse, but variable, correlation between plasma RNA and the level of CD4+ lymphocytes (McFarland, 2005). With the use of HAART, we see an increase in CD4+ number and a decrease in plasma RNA. According to the classification system introduced by The Centers for Disease Control and Prevention in 1994, children between the ages of six and 12 years, with a CD4+ count of greater or equal to 25%, show no evidence of immune suppression.

### **2.3 Classification of Paediatric HIV Infection**

The Centre for Disease Control and Prevention (1994) established a classification system for children with HIV based on their clinical and immunologic status. The clinical classification consists of four groups: stage N- no signs and symptoms; stage A- mild signs and symptoms (examples hepatomegaly, splenomegaly, lymphadenopathy, and recurrent otitis media); stage B- moderate signs or symptoms (lymphoid interstitial pneumonitis is the only AIDS defining illness included in this category); stage C- severe signs and symptoms ( including all other AIDS defining conditions). It has been noted that some children can pass from stage N to stage C directly.

The WHO (2007) has implemented its own classification system, similar to that of the Centre for Disease Control, with children classified by Clinical Stages One to Four. Stage 1 indicates no symptoms present; stage 2: mild symptoms present; stage 3: child displays advanced symptoms and stage 4: child displays severe symptoms. The medical conditions associated with each stage are extensive (WHO, 2007).

Immunological status has been described by the Centre for disease control (CDC, 1994). This is described in the table below:

Immunologic categories based on age-specific CD4+ T-lymphocyte counts and percent of total lymphocytes

Immunologic category	Age of child					
	<12 mos		1-5 yrs		6-12 yrs	
	uL	(%)	uL	(%)	uL	(%)
1: No evidence of suppression	≥1,500 (≥25)		≥1,000 (≥25)		≥500 (≥25)	
2: Evidence of moderate suppression	750-1,499 (15-24)		500-999 (15-24)		200-499 (15-24)	
3: Severe suppression	<750 (<15)		<500 (<15)		<200 (<15)	

## 2.4 Highly Active Antiretroviral Therapy

The goals of HAART in paediatric patients with HIV are fourfold: to achieve viral suppression; restore or preserve immunological function; sustained improvement in clinical symptoms and reduction in morbidity and mortality and consequently improve quality of life (Cotton et al, 2009; Havens, 2003). Without HAART intervention, the large majority of infected children would die before their fifth birthday (Newell et al, 2004). A combination of three or more antiretroviral medications has been recommended replacing the original monotherapy previously advocated (Havens, 2003). All infants younger than twelve months should receive HAART irrespective of immunological status (Cotton et al, 2009). This is to reduce the rates of encephalopathy and rapid disease progression

(Havens et al, 2003). Babies older than twelve months should begin HAART even with mild symptoms associated with HIV( Category A on CDC classification) (Havens, 2003).The benefits and guidelines regarding the initiation of HAART based on CD4 levels only, in an asymptomatic child, remains inconclusive (Havens, 2003). In sub-Saharan Africa, since 2003, coverage of HAART has improved from only 2% to 40% (Harries et al, 2010). HAART should include category II nucleoside reverse transcriptase inhibitors (NRTI) as well as a category III non-nucleoside reverse transcriptase inhibitor (NNRTI) (Dep.of Health, 2010). Guidelines published in 2010 advocate the initiation of HAART for all babies younger than one year, children aged one to five years who are symptomatic (stage III or IV) with absolute CD4+ <750 cells/mm<sup>3</sup> and those older than the age of five who are symptomatic and with absolute CD4+ <350 cells/mm<sup>3</sup> (Dep. of Health, 2010). Preferred regimen for children younger than three or weighing less than 10 kg is Abacavir, Lamivudine and Lopinavir/Ritonavir. For children older than three and weighing more than 10 kg, Abacavir, Lamivudine and Efavirez is preferred (Dep. of Health, 2010).

Despite the significant decrease in mortality, morbidity and hospitalization rates seen with the use of HAART in paediatric patients (Gortmaker et al, 2001), this comes at a cost of a plethora of side effects associated with antiretroviral medication use (Brown et al, 2010; Cotton et al, 2009; Aldrovandi, 2005; McKinney, 2005; Havens, 2003). These include: hematological (anemia and neutropenia), gastrointestinal (diarrhea, vomiting, nausea), myopathies, neuropathies, hyper pigmentation, fatigue, hepatitis and skin rashes (McKinney, 2005). Lipodystrophy has also been reported (Cotton et al, 2009). The extensive short- and- long term side effects noted with HAART, has raised the issue of replacing the morbidities associated with immuno-suppression with those associated with antiretroviral toxicity (Aldrovandi, 2005). Non-adherence to HAART and the consequent emergence of a drug-resistant HIV strain and a detectable viremia remains a challenge to health workers and patient alike (Brown et al, 2010; Havens, 2003).

## **2.5 Adherence to HAART in Paediatric Patients**

Adherence to HAART remains a challenge for HIV-infected adults, children and their health workers. In a review of studies analyzing adherence of paediatric patients to HAART, Mellins et al (2004) found that rates of adherence ranged from 57 to 81%. These rates of adherence are not conducive to long-term viral suppression and treatment (Mellins, 2004).

Looking at sub-Saharan Africa specifically, in relation to adherence success, data was found relating to adult adherence. Rosen et al (2007) in their literature review found that only 60% of adults continued with their antiretroviral medication longer than 2 years after initiating therapy. The main causes of non-adherence cited included death and loss to follow-up. In research conducted in the Eastern Cape region of South Africa, using adults living in rural and urban environments, barriers to adherence were found to be social stigma, amount of support from family and friends, accessibility to medication and long standing racial misconceptions from the apartheid era (Mitchell et al, 2009). In the National Antiretroviral Treatment Guidelines (Department of Health, 2010), both medical and psychosocial criteria are specified for eligibility of antiretroviral therapy for children and adults. The caregiver/parent has to demonstrate reliability by attending clinics regularly and should have a support network in place including another adult who is aware of the child's HIV status.

From the research, a picture is emerging as to the barriers of effective paediatric adherence. Levels of adherence are not only influenced by the child and his/her immediate environment but also factors that are beyond their control. The use of HAART introduces a life-long daily use of multiple, often unpalatable, medications administered at required specific times. The medications require specific storage requirements and precise dosage. In addition to this are the many previously mentioned long-term and short-term side effects associated with

the use of HAART. These factors in themselves form a barrier to effective adherence (Simoni et al, 2007; Steele et al, 2007; Mullen et al, 2002).

For some patients access to health services to obtain the medication remains difficult from an economic perspective and distance required to travel to clinics. The health-care workers themselves may create a barrier if they are poorly trained and have ineffective communication skills with the children and caregiver (Simoni et al, 2007). Neglecting to take into account the belief and cultural norms of the child and his/her family, will influence patterns of adherence (Steele et al, 2007). Payment for therapy and its effect on adherence was analysed in Biadgilign et al (2008) who found that adherence amongst their cohort in Ethiopia decreased if the medications were obtained for free.

Due to the reliance of the younger child on a parent or caregiver for medication, family/caregiver factors are crucial to adherence success (Simoni et al, 2007; Steele et al, 2007; Mellins et al, 2004). Numerous familial and social factors have been shown to influence adherence. Decreased caregiver quality of life, increased stress experienced by child and caregiver, limited social support and lower family socio-economic status and stability all affect adherence negatively (Simoni et al, 2007; Steele et al, 2007; Mellins et al, 2004). A positive relationship with good communication between child and caregiver responsible for administration of HAART will improve rates of adherence (Steele et al, 2007). As HIV encephalopathy and cognitive impairment are still features associated with HIV, despite HAART, Malee et al (2009) set out to assess the impact cognitive functioning has on adherence. Impaired cognitive functioning in the child does not appear to influence rates of adherence (Malee et al, 2009)

Disclosure and its effect on adherence remain inconclusive in the literature. Steele et al, 2007 report that non-disclosure affects adherence negatively. However further research remains to be done in developing world environment where disclosure appeared to decrease adherence in a cohort in Ethiopia

(Biadgilign, 2008). This research also indicated the negative impact on adherence when the child became aware of his caregiver's positive HIV status. Disclosure will be referred to, in greater detail later in the literature review. Demographic data such as caregiver education and caregiver marital status are not predictive of adherence or non-adherence (Mellins et al, 2004).

## **2.6 HIV Related Central Nervous System Disease in Children and Associated Motor and Cognitive Development**

The central nervous system may be affected by the HIV virus directly or indirectly. The mechanism of indirect involvement is via opportunistic infections, malignancies and cerebrovascular disease (Civitello, 2005). The direct neurological and developmental effects of HIV and AIDS in HIV-infected infants and children, by the virus crossing the blood-brain barrier, has been described extensively in the literature (Mitchell, 2006; Belman, 1992; Epstein et al, 1986). Three patterns of HIV- related CNS involvement have been suggested by the Working Group of the American Academy of Neurology AIDS Task Force (1991) and Wolters and Browsers (2005)

### **1. HIV-related Encephalopathy**

It is characterised by acquired microcephally, global impairments in cognition, language (expressive more than receptive), pyramidal tract motor deficits, hypertonicity (lower limbs affected more than upper limbs), and loss of social skills. The encephalopathy has been further categorised into a progressive, or a static encephalopathy (Mitchell, 2006; Wolters and Browsers, 2005; Mitchell, 2001). Progressive encephalopathy was the most commonly seen neurological manifestation in the pre-HAART era (Mitchell 2006) and was often seen as an AIDS defining illness in a large percentage of children. With the introduction of HAART, the incidence of severe forms of encephalopathy has been reduced (Patel et al, 2009; Mitchell, 2006) however HIV infection in-utero still poses a risk of encephalopathy development (Bomba et al, 2010). In their study, Patel et al (2009) found a decrease in the incidence of encephalopathy by 50% with the use of HAART.

By 2007, an UNAIDS progress report for South Africa stated that only 36% of children with advanced AIDS living in South Africa were receiving HAART (Zanoni, 2009). From this data one can assume that the associated motor and cognitive delays associated with encephalopathy are still plaguing the sub-Saharan paediatric HIV population.

## **2. HIV-Related CNS compromise**

Children included in this category include those with overall cognitive functioning within normal limits but at the low range of normal. They may display some neurobehavioral limitation but are still able to cope in the mainstream school environment and with daily activities of living. The early administration of HAART is associated with the emergence of CNS compromise as opposed to the severe forms of encephalopathy noted prior to the HAART era (Wolters and Browsers, 2005). HAART has been less effective in reducing the more subtle forms of encephalopathy due to the fact that viral replication may continue in the central nervous system (Mitchell, 2006). Research on the effect of HAART on neurodevelopment has focused on children below three years of age. However there is a need for more research on older children (Earls et al, 2008).

## **3. Apparently not affected**

Cognitive functioning is at least within the normal range. No neuro-behavioural domains appear affected or show signs of deterioration (Wolters and Browsers, 2005).

Cognitive development refers to the process of reaching developmental milestones, language development, intelligence, and emergence of appropriate behavioural and socialization skills. The varied and extensive measurement tools used to assess cognitive development may concentrate on different clusters of skills (Sherr et al, 2009). Research pertaining to the cognitive development and functioning in children falling into category two and three, i.e. children with CNS compromise and apparently not -affected, remains inconclusive. Small sample size, inconsistent measurement tools, varying ages of children, stage of



disease, inconsistent HAART regimes, and varied control groups all contribute to the complexity of analysis and interpretation of research results (Sherr et al, 2009; Martin et al, 2006). Furthermore, factors such as poverty, gender, race, and exposure to drugs cannot be eliminated as contributing factors to the cognitive development in children with HIV (Sherr et al, 2009).

Since the introduction of Intelligence Quotients (IQ) in 1905, they have been used and accepted as adequate measures of intelligence and cognitive functioning. A Full Scale Intelligence Quotient (FSIQ) of  $\geq 90$  and  $\leq 110$  is considered average. Children scoring consistently below 70 on the FSIQ are considered to have mental retardation (Gillberg, 2006).

In an attempt to analyse the direct effects that HIV might have on cognitive development, researchers have attempted to find a link between cognitive development and various factors such as disease stage, extent of radiological changes and disease progression. Martin et al (2006) found that the majority of HIV-infected school-going children, in his sample, were functioning within the normal range of average FSIQ, albeit at the lower end of this range. However Nozyce et al (2006), using the same measurement tool as Martin et al (2006), found that their sample of HIV- infected children functioned at a lower cognitive level than that considered normal for the general population.

Smith et al (2006), were able to link the extent of cognitive deficit to stage of disease, whereby it was found that children in category C (according to the CDC Classification), had lower overall scores on cognitive testing. Verbal skills, perceptual- performance, quantitative abilities and memory were shown to be most affected in this cohort of children. They further demonstrated that HIV positive children, without an AIDS defining illness (category A or B in CDC classification), performed at the same cognitive level as uninfected children of the same age.

The direct relationship between radiological changes on computerized tomography (CT) scans of the central nervous system and cognitive development and functioning has been documented by Blanchette (2001) and Martin et al (2006). Children with CT scans, identified as within normal limits, performed as their non- infected peers, following a normal curve seen in FSIQ. In contrast children with mild to moderate changes were functioning cognitively at a lower level. The specific domains that were assessed in this research were working memory, logical sequencing and planning, attention to visual detail and visual-spatial organization (Martin et al, 2006).

A direct correlation between CD4+ percentages, viral load and cognitive development of children receiving HAART has not been established (Martin et al, 2006).

The influence of socioeconomic status, race and mode of HIV transmission as independent variables, in the cognitive development of HIV-infected children needs to be considered. In Martin et al (2006) and Nozyce et al (2006) previously mentioned, the majority of the children were from different demographic groups. In Martin et al (2006) the majority of the children were white children (54%), whereas in Nozyce et al (2006) only 15% of the children were white and the majority of the children were African American. However in neither of the research projects was socioeconomic status of the sample defined or suggested as an influencing factor on cognitive development. No distinction is made on mode of HIV infection.

Despite the appearance that many of the school going HIV-infected children are functioning within normal limits cognitively, a large percentage of infected children might require additional educational and psychological interventional resources (Lourie et al, 2005). This might be due to the fact that when assessed on individual subtests of cognitive functioning, as opposed to FSIQ, clear deficits, as compared to uninfected peers, are recognised (Martin et al, 2006). The benefit

of assessing FSIQ only is therefore questionable in the population of HIV-infected children.

The majority of research on the cognitive development in HIV-infected children has centred on American children as study participants (Sherr, 2009). The results of this research may not be able to be generalised to children living in poorer environments and highly endemic regions such as South Africa. In their review of the literature pertaining to cognitive and motor development of HIV infected children in Sub-Saharan Africa, Abubaker et al (2008) found a lack of relevant data pertaining to children over the age of two. Cognitive delay in South African HIV-infected children, younger than three, has been demonstrated by Potterton et al (2009) and Baillieu and Potterton (2008) using the Bailey Scales of Infant Development (2nd edition). The children assessed were HAART naïve but for a small number of children in Potterton et al (2009) receiving antiretroviral therapy. Further research on cognitive development in South Africa is needed looking at the population of children that have received antiretroviral therapy from an early age. The early initiation of HAART, preventing an AIDS defining illness, is of crucial importance in optimising the cognitive development of children with perinatally transmitted HIV (Smith et al, 2006).

There is no data available at present analysing the cognitive development of vertically infected school-aged children in South Africa. In a small study from Uganda, the cognitive development of HIV infected school-aged children was found to be within normal range with respect to the neurological and psychometric measures used. These children were all HAART naïve and were not exposed to illicit drugs (Bagenda, 2006). However in the review of this study, it was noted that only 40% of HIV-infected children survived their fourth birthday, suggesting a very limited sample with only the minimally affected children remaining in this cohort (Earls et al, 2008).

The development of children in high- prevalence countries is already compromised by impoverished conditions (Chandan and Richter, 2009; Earls et al, 2008), making it harder to assess the extent of the direct effects that HIV infection may have on cognitive development. Factors relating to poverty, that have a varying effect on intellectual/ cognitive development in children with HIV, include amount of cognitive stimulation in the home, parenting style, physical environment, child health at birth, and childhood health (Guo and Mullen Harris, 2000). Other factors identified by Smith et al (2006) that were associated independently with lower cognitive scores in their cohort of children included maternal education and child gender.

Gross motor development in HAART naive vertically infected –HIV children, proves to be more compromised than their cognitive development (Potterton et al, 2009; Baillieu and Potterton, 2008; Drotar et al, 1997). The above mentioned authors have attributed the delay to the presence of generalized weakness and/or encephalopathy associated with vertically transmitted HIV. These findings corresponded to those of Smith et al (2002) who found similar findings in children in a developed country environment, indicating that the motor delay is not associated with environmental factors but rather the direct effect of HIV infection.

## **2.7 Growth Patterns in Children with HIV**

HIV has been associated with negative long-lasting disturbances of height and weight in vertically infected children and these two parameters are often used as indicators for prognosis (Isanka et al, 2009; The European Collaborative Study, 2003; Hirschfeld, 1996). This disturbance in growth patterns is found in developed and developing countries alike, indicating the direct association between HIV infection and growth (Storm et al, 2005). It is more common to find children who have a stunted growth pattern (decreased height for age) as compared to a pattern of wasting (decreased weight for age) (Isanka et al, 2009; Nachman et al, 2005; Hirschfeld, 1996). Growth disturbances can be noted as early as three months and continue into childhood, becoming more marked with

age. From the age of two years and four years respectively changes in the height and weight patterns of HIV-infected children become more obvious. On average HIV-infected children, at age ten, were found to be seven kilograms lighter and seven and a half centimetres shorter than a control group and the average of the general population (European Collaborative Study, 2003). In the analysis of growth disturbances in HIV-infected children it is necessary to eliminate socioeconomic factors as a confounding factor. This was achieved by The European Collaborative Study using a control group of children born to a HIV positive mother but uninfected. These children were found to have no difference in growth patterns to the national average for children living in Britain. Additional information garnered from this study included the finding that HIV- infected children in category C (CDC classification system) appeared to have more marked growth disturbances than those children in category A and B.

Several causes have been proposed for the poor growth namely: (1) repeated infections associated with HIV/AIDS, (2) insufficient caloric intake usually due to socioeconomic reasons, (3) decreased absorption of food in the gastro-intestinal tract and (4) increased energy utilization during HIV replication process (Kabue et al, 2008). This would account for the fact that growth disturbances have been noted in children from both developed and less developed countries (Isanka et al, 2009).

HAART has been shown to have a positive effect on growth dysfunction, with both parameters increasing even in a resource poor setting like Uganda (Kabue et al, 2008; Nachman et al 2005). Nachman et al (2005) have noted that the positive effects that HAART have on the weight of the child responds quicker than the height. Combination therapy appears to have a greater effect on improving growth parameters than monotherapy, but more research is required to pinpoint the exact regimes which would prove to be more effective (European Collaborative Study, 2003).

## **2.8 Psychosocial Well-being and Adjustment of HIV-Infected Children**

For all children, the healthy development of psychological and social functioning is influenced by the presence of a caring and nurturing caregiver, appropriate peer relationships, play, schooling and cultural influences (Richter et al, 2006). Ultimately children are required to learn the appropriate behaviours and values accepted in their communities.

Chronic paediatric diseases are known to create psychological and social burdens on a child and their family (Bauman et al, 1997). In their definition of psychosocial wellbeing of children affected by HIV/AIDS, King et al (2009) look at the emotional status of the child, their ability to adjust to their social environment and the combination of the two factors. A child infected with HIV, will face many social challenges such as illness or death of a parent, stigma, disclosure, possible isolation, additional responsibilities in the family, economic constraints and the negative side effects of HAART. For that child to be able to adjust and fully participate in their family and society, now and in the future, he will require the social, emotional, motor and cognitive skills appropriate for his age (King et al, 2009; Richter et al, 2006). The ability of the child to cope and adjust to living with a chronic condition becomes vital for his psychosocial well-being. Using the definition suggested previously by Wallender and Thompson in 1995, Wallender and Varni (1998) described a child to be well adjusted if he displays behaviour which is socially acceptable, age appropriate and facilitates future positive adult behaviour. Mal-adjustment is associated with clinically pathological and age inappropriate behaviour.

In summary, psychosocial adjustment will be influenced by numerous factors. A child's ability to cope and respond positively to high levels of stress will depend on temperament, personality type and effectiveness of coping mechanisms utilised (Richter, 2004). Factors, often beyond the control of the child, affecting psychosocial adjustment include: medical status, disclosure or non-disclosure,

negative life events, availability of social support, familial environment and relationships (Steele et al, 2007). In the following paragraphs the author will be discussing information relevant to the psychosocial well-being of the child infected with HIV.

## **2. 9 Psychiatric and Behavioural Disorders associated with HIV**

It has been well established that chronic childhood diseases are associated with increased, clinically observable, emotional and behavioural problems (Gannoni and Shute, 2010; Scharko, 2006). HIV is no exception with the psychological effects ranging in severity (Mellins et al, 2003). Children vertically infected with HIV would appear to be at even a greater risk of developing psychiatric and behavioural problems due the effects of the virus crossing the blood-brain barrier, potentially neurotoxic antiretroviral medication and growing up in a disadvantaged household (Gadow et al, 2010; Nozyce et al, 2006).

Increased levels of anxiety, depression, attention deficit hyperactivity disorder (ADHD) and conduct disorders have all been observed in the HIV-infected paediatric population (Chernoff et al, 2009; Nozyce et al, 2006; Scharko et al, 2006; Mellins et al 2003). However the direct association between HIV and an increase in psychiatric and behavioural problems remains unclear. Mellins et al (2003) and Chernoff et al (2009), from their study comparing HIV infected children and a control group (perinatally exposed but uninfected children and children living in a house with one infected individual, similar demographic characteristics), found no statistical differences between study and control groups with reference to rates of psychiatric and behavioural problems. Both groups reported higher incidence of psychiatric and behavioural problems than the general population. Mellins et al (2003) argue that it is the demographic characteristics and environmental factors associated with the epidemiology of paediatric HIV disease that predispose the child to higher than normal levels of psychological and behavioural problems (particularly ADHD) - not the HIV infection directly. These factors included family disruption, exposure to poverty,

trauma, ongoing parental drug abuse and familial mental illness in the home. In this research no mention was made of whether children were receiving HAART or at what stage of the disease process they had been classified.

In his review of the literature pertaining to rates of behavioural and psychiatric conditions in HIV-infected children, Scharko (2006), noted the small samples of children used in research studies, the variance in ages and mode of infection (boys with haemophilia used), and the lack of adequate controls . These limitations in studies were addressed by Gadow et al (2010). In their study of 319 HIV positive children, age, medical status and HAART were all controlled. Their findings indicated no increased incidence of psychiatric conditions in the HIV-infected children as compared to the control group (psychiatric conditions assessed included ADHD, conduct disorder, oppositional defiance disorder, generalized anxiety, depression and manic episodes). Two statistical differences however were found between the study and control group namely: (1) a higher rate of somatisation symptoms reported by the HIV-infected children and (2) use of pharmacological interventions for emotional and behavioural problems was higher in HIV –infected children. The limitation remaining in the research include: (1) selection criteria for HIV-positive children were not standardised, (2) wide ranges of age groups were used, (3) the control group included uninfected children born to HIV positive mothers exposed to possibly neurotoxic antiretroviral medication and (4) the socioeconomic factors and their influence on development of children are always confounding factors.

Research indicating an increase in behavioural and psychiatric conditions associated with HIV (Nozyce et al, 2006), did not use a control group to compare results. Wolters and Browers (2005) concluded that behavioural problems in HIV-infected children may be attributed to a combination of central nervous system involvement related to HIV infection, the psychological stress associated with chronic illness, biological, environmental and genetic factors.



In an attempt to link changes seen on neuro-imaging of the central nervous system, CD4+ counts and behavioural manifestations such as ADHD, conduct and anxiety disorders, Nozyce et al (2006) found no evidence of this. However, only 12% of the children in the cohort had structural changes visible on CT scan. In only Mellins et al (2009) a positive association was found between HIV-positive adolescents and an increased incidence of ADHD as compared to a control group. Again, both study and control groups demonstrated higher levels of psychiatric dysfunction than the accepted rates of the general population of inner city youth of the same age and adolescents with chronic conditions. These adolescents represented a group of HIV-infected children born prior to the accepted use of HAART and many psychiatric conditions are known to emerge during this developmental stage. Mellins et al (2009) have recommended further research to identify the possible aetiology of increased prevalence of ADHD in HIV-positive adolescents.

No research was found pertaining to the South African HIV-infected paediatric population. However in Mellins et al (2003) and Gadow et al (2010), children in the study lived in lower socioeconomic conditions, almost half of the mothers had not completed high school at time of birth and had a low yearly income. Findings of this research may then have some value to our population. In South Africa, other factors beside socioeconomic conditions might influence behavioural and psychological functioning in children. The legacy of apartheid with its associated ramifications on family structure and the associated violence still experienced in the communities might play a role. In a study comparing South African and similarly matched African American six year olds, all non HIV infected, it was found that South African children were less likely to display anxiety, depression and hyperactivity but displayed more antisocial and disruptive behaviours (Barbarin, 1999). The South African sample was predominantly black children living in Soweto.

Understanding the causes of behavioural problems in children with HIV is vital as the appropriate interventions are needed to ensure an improved quality of life for these children (Mellins et al, 2003). Treating behavioural and psychiatric conditions may also have the effect of improving adherence to HAART (Mellins et al, 2003). Irrespective of the underlying aetiology of the behavioural and psychological patterns manifesting in HIV-infected children, management of the symptoms is vital to ensure an improved quality of life (Brown et al, 2000).

Psychological and behavioural dysfunction in children with HIV can be treated with psycho-stimulants, antidepressants, antipsychotics, anticonvulsants and mood stabilisers. Being HIV positive might in-fact increase the child's chances of intervention, especially in resource-poor communities where many uninfected children might go untreated due to a lack of medical and or psychological facilities. This was evident in Chernoff et al (2009) who found that a higher percentage of HIV positive children were receiving an intervention as compared to non-infected children despite both groups reporting a high rate of behavioural and psychiatric conditions.

Drug interactions have been noted between the traditionally used psychiatric medication cited above and HAART (Lourie et al, 2005). Close monitoring of the child and consultation with family is essential to avoid the negative drug interactions.

## **2.10 Disclosure**

With the introduction of HAART and its effect on increasing survival rates of children infected vertically with HIV, the burden of disclosure has become a reality for many parents and care-givers (Wiener et al, 2007). Patterns of disclosure include non-disclosure, partial disclosure and full disclosure, with partial disclosure being recommended for the younger child (Weiner et al, 2007). Disclosure should not be viewed as a once off event, but rather as a process that

might continue over a period of time, moving from non-disclosure to complete disclosure (Wiener et al, 2007; Lester et al, 2002).

The ideal age of disclosure remains elusive, with no specific age emerging as the most appropriate (Wiener et al, 2007; Mellins et al, 2002). It is evident that age is not the overriding factor determining rates of disclosure but rather many psychosocial factors relating to the child and his family. It is the opinion of the American Academy of Pediatrics' that all children and adolescents, infected with HIV, should be informed of their status (1999). However this was based on their research on children diagnosed with various forms of cancer and the disclosure thereof. It is difficult to compare HIV to paediatric cancer as the medical outcomes and social factors are not similar.

Disclosure remains a challenge due to the stigma associated with HIV/AIDS, not only for the child but for the family as a whole (Brown et al, 2010; Lesch et al, 2007; Lester et al, 2002; Mellins et al, 2002). Disclosure of the child's positive status will ultimately lead to the disclosure of the HIV status of the biological mother. Wiener et al (2007) , in a review of research conducted by Flanagan-Klygis et al (2001), Waugh (2003), Mellins et al (1994) and Wiener et al (1996), found that there are a variety of reasons which consistently prevent parents from making full disclosure to their children. These included age and maturity level of the child, the fear of the diagnosis being revealed to family and friends, stigmatisation and anger from the child and possible depression. For some caregivers/ parents, the deteriorating health status of the child might influence their decision to disclose to the child and others. As the treatment regimes require greater degree of adherence from the child, disclosure might become inevitable (Mellins et al 2002). It is often the child's questioning about his health and medication that prompts the need for disclosure (Lester et al, 2002). The relationship of trust between caregiver and child may be compromised by prolonged non-disclosure (Wiener, 2005).

A parent contemplating disclosure to their child will need to consider their child's age, cognitive abilities, emotional development, location of disclosure, their familial cultural norms relating to health and dying, and the content of information to be disclosed (Weiner et al, 2007; Wiener, 2005). A concern that parents have expressed with regard to disclosure is the fear that death and dying might become a preoccupying thought for their children with consequent negative effect on their psychosocial adjustment (Lester et al, 2002). This cannot be confirmed by the literature as research regarding the psychosocial impact that disclosure has on children with HIV remains inconclusive (Wiener et al, 2007). Whilst some research has found that less secrecy promotes improved psychosocial functioning of the child and the caregivers (Brown et al, 2010), there is also a body of literature that states that disclosure has a negative impact or no impact on the child (Wiener et al, 2007). Butler et al (2009) found that disclosure did not impact negatively on the quality of life of children with vertically transmitted HIV.

Mellins et al (2002) strongly recommend that by early adolescence all children should be aware of their HIV positive status. It has been suggested that all adolescents and children requiring hospitalisation should be informed of their status with the appropriate amount of information for their age, so as to prevent inadvertent disclosure by medical staff (Brown et al, 2010).

There is limited research that has been done regarding age patterns of disclosure in South Africa. Moodley et al (2006), in their study in Cape Town, found that the majority of caregivers in their cohort felt that the age of 12 is the ideal age to disclose to the child. This contrasted with the opinion of healthcare-workers, at a tertiary outpatient HIV clinic, who felt that at the age of 10 was the correct age for disclosure (Myer et al, 2006).

The National Education Policy Act of 1996 prohibits any discrimination against attendance/entrance to school, forced testing and/ or disclosure. Disclosure of

child's status can only be done with the caregivers and child's consent (when age appropriate). The policy advocates that a child older than 14 is able to disclose his/her status without parental consent.

There are many moral, ethical and legal ramifications to a parents' decision on disclosure. The issues of adherence, creation of drug resistant strains of HIV and sexual transmission are all issues that children with HIV will have to deal with as they enter adolescence (Frederick et al, 2000). Whether they are aware of their positive status has enormous ramifications in our society.

### **2.11 Coping Mechanisms and Psychosocial Adjustment**

Children utilise various coping mechanisms to adjust to living with HIV/AIDS (Steele et al, 2007). Research on coping mechanisms employed by children diagnosed with a chronic illness and their families, has largely been based on conditions other than HIV (Martin et al, 2004). Lazarus and Folkman, in 1984, suggested that children may utilise either emotion-focused or problem-focused coping mechanisms (Martin et al, 2004). Their definition of the above, as cited by Martin et al (2004), states that children using emotion-focused coping mechanisms believe that their situation cannot be changed and avoidance techniques are utilised. This may be seen as a more passive form of coping (Martin et al, 2004). Children with problem-focused coping skills are able to see that a stressful situation is changeable and they generate solutions and learn new skills. This is a more active form of coping (Martin et al, 2004). It has been found that children using the more passive, emotion-focused strategy report more emotional and behavioural problems (Steele et al, 2007).

One cannot examine the coping skills of a child in isolation. They function as part of a family system and hence are influenced by the family and coping mechanisms they employ. In their research on coping mechanisms employed by the families of children infected with HIV, Martin et al (2004) found three main patterns of coping mechanisms namely: avoidance (handing over responsibility

to health workers ) ; spiritual reinforcement; and seeking out social support from outside the family. Due to the associated stigma of HIV/AIDS, use of external social support was used less as a coping mechanism by the families. It appears that a reciprocal relationship often develops between the child infected with HIV and their family. The coping mechanisms employed by the family will affect the child's psychological, developmental and medical functioning (e.g. extent of adherence) and in turn the child's functioning in the above mentioned areas will influence the family on choice of coping mechanisms employed (Martin et al, 2004).

### **2.12 Family-Centred Intervention and Psychosocial Adjustment**

The role of the family in the psychosocial adjustment of the HIV-infected child has been substantiated from all the above information. The effects of a caring and nurturing environment and family can only promote the resilience that children are known to possess (Richter et al, 2006). The family can be identified as an open system which will have a large influence on the child's behaviour and development. A healthy family system will be able to adapt to and withstand negative external and internal stressors such as ill-health (Malcolm, 1998). It therefore stands to reason that interventions aimed at improving the psychosocial adjustment of the HIV-infected child, and consequently their quality of life, should be aimed at the family unit and not the individual child only. Family-based interventions aim to strengthen the family system thereby empowering them to make and find positive solutions to the stressors experienced by the child, thereby improving his health and quality of life (Malcolm, 1998).

### **2.13 Socioeconomic Factors Affecting HIV-Infected Children in South Africa.**

The Poverty Line denotes a monthly/weekly income that separates the poor from the non-poor. An income classified to be below the poverty line limits full participation in society and attainment of a healthy life style (Van der Berg et al

2007). In South Africa the poverty line has been set at R250/per month or R3000/ year (Van der Berg et al 2007).

Throughout the review poverty has been mentioned as a confounding factor in the effects of HIV on children. With poverty being so widespread in countries where HIV is found in so prevalently, it is often difficult to distinguish between the direct effects of HIV on the health of the children (Richter, 2004). Richter (2004) questions whether we should in fact be focusing solely on the HIV/AIDS epidemic and its affected individuals OR on poverty as a whole with the focus being on more widespread interventions directed at social institutions.

It is the poorest South Africans that are most affected by the HIV/Aids pandemic and the consequences for them are often dire. For many, HIV/AIDS has changed the family's economic position from poverty to destitution (Steinberg et al, 2002). In a survey by Booysen and Bachman ( 2002), as cited by Andrews et al (2006), it was found that families with at least one infected member had a monthly income half that of the unaffected households. Consequent to HIV/AIDS, altered family dynamics, foster care, living with ill parents, poor access to health care and nutritional deprivation have all been seen as socio-economic factors affecting children and consequently their QoL (Missmer, 2000).

The death of a parent or caregiver may have a twofold effect on the child, namely financial implications and an emotional loss. More time spent with a caregiver has been associated with a more positive QoL in children (Xu et al, 2010).

Financially, already limited resources may be further compromised with a resultant negative impact on the child's health, and educational opportunities (Desmond, 2009; Andrews et al, 2006). Research in South Africa has looked at school enrolment of HIV orphans and non-orphans affected by HIV/AIDS. Orphans have been shown to have reduced access to education and a higher drop-out rate (Andrews et al, 2006).

It has been stated that the loss of a mother has a greater impact on the child's care than the loss of a father (Desmond, 2009). In South Africa, the pattern of female headed single parent households and the ramifications of Apartheid on family structure are well established (Petersen et al, 2010; Andrews et al, 2006). In the poorer communities, children and their fathers often do not reside together for a variety of reasons, and female headed households are very common (Desmond and Desmond, 2006). According to the General Household Survey of 2002, a father is present in only 48% of households and a mother in 80% of households (Statistics SA, 2002). It is however not accepted that only a nuclear family may be considered to be an effectively functioning family system (Malcolm, 1998). A strong and supportive family with good access to effective services can minimize the effects of HIV/AIDS on children (Desmond, 2009). He continues by saying that it is rather the failure to respond to poverty that allows HIV/AIDS to continue its negative impact on our children.

## **2.14 Quality of Life**

With HIV/AIDS it has become essential to treat the child holistically, looking at their adjustment to the illness and its treatment (Harding, 2001). An additional health measure, QoL, has become essential to evaluate intervention outcomes for children with HIV/AIDS (Garvie et al, 2009; Lee et al, 2006; Missmer et al, 2000; Wallender and Varni, 1998).

Quality of Life (QoL) has been defined by the WHO as "the individuals' perception of their position in life in the context of culture and value systems in which they live, and in relation to their goals, expectations, standards, and concerns." (WHOQOL, 1997 page 1). The quality of life of the individual is influenced by their physical health, psychological state, level of independence, personal relationships, beliefs, and environment (WHO, 1997). Quality of life defines all aspects of a patients' well being transcending the medical model (Berzon, 1998)



The concept of Health Related Quality of Life, as a separate construct, was originally created to distinguish between the outcomes in health related research and sociological research on healthy populations (Smith et al, 1999). Health related Quality of Life (HRQoL) is distinct from QoL in that it examines the perceived effect that illness and subsequent medical intervention has on the varying facets of life, not only physical functioning ( De Civita et al, 2005). It reflects the holistic nature of the Classification of Function, Disability and Health adopted by the WHO in 2001.

Many authors have attempted to define the concept of HRQoL but with no single definition emerging in the literature (De Civita et al, 2005). Despite the numerous definitions there are common themes that emerge. HRQoL is a subjective appraisal of the impact a disease or condition might have on the functioning of an individual. Functioning includes the physical, psychological and emotional well-being of that individual and his/her ability to participate in their family and community in a meaningful way. It further looks at the individuals' perception of their medical status and the effectiveness of the treatment and interventions they are receiving (Wallender and Varni, 1998; Shumaker and Naughton, 1997; Eiser, 1996). Domains of social, physical and cognitive functioning; mobility and self-care; and emotional wellbeing are critical in any evaluation of HRQoL (Shumaker and Naughton, 1997). Evaluating HRQoL requires a two-fold approach for it to be meaningful and appropriate. Both the functional impact a medical condition, or treatment thereof, has on the above mentioned domains, and the child's perception of the effects on the domains needs to be considered (Waters et al, 2009; De Civita et al, 2005). A third construct described in the literature in association with QoL and HRQoL, is health status. A clear distinction however can be drawn between QoL, HRQoL and health status. Health status refers uniquely to the patient's perception of their physical functioning only (Garvie et al, 2009; De Civita et al, 2005). Health status therefore bears no significance to this research.

The medical literature appears divided as to the use of the terms QoL and HRQoL as separate constructs. Authors have found that the terms are often used interchangeably (Clayson et al, 2006; Smith et al, 1999; Wallender and Varni, 1998) despite recommendations to the contrary (Davis et al, 2006; Shumaker and Naughton, 1997).

### **2.15 Quality of Life of Children with Chronic Diseases**

Living with a childhood chronic disease and the impact thereof on HRQoL has become an important research topic in the developed world. Colver (2008) warns against assuming that impairment or loss of function would automatically result in a child reporting a lower QoL. However extensive research in this field has shown, to varying extents, the negative effect of a chronic childhood condition on HRQoL (Grootenhuis et al, 2008; Janssens et al, 2008; Maher et al, 2008; Van Der Lee et al, 2007; Williams et al, 2005; Sawyer et al, 2004; Powers et al, 2003; Varni et al, 2002). It is beyond the scope of this literature review to discuss specific chronic childhood conditions and their effect on HRQoL.

A child living with a chronic disease might not be able to achieve the developmental milestones, motor and cognitive, usually achieved by other children. This might have a resultant effect of increased dependence on parent/caregiver and limitations in peer-interaction and school-based activities. These limitations in participation have been shown to affect HRQoL of children living with a chronic condition (Grootenhuis et al, 2008). Areas of functioning that have been shown to be affected by a chronic condition, with a consequent decrease in reported HRQoL, include the physical, emotional, cognitive and social aspects of a child's life (Grootenhuis et al, 2008; Williams et al, 2005). Due to the differing medical conditions assessed, different inclusion and exclusion criteria and measurement tools used in the research, it remains difficult to analyse which of the above aspects of functioning contribute the most to a lower reported HRQoL in children with a chronic condition.

In young people living with a chronic condition, HRQoL is dynamic (Taylor et al, 2008). HRQoL will continuously shift, not always negatively, depending on the child's developmental stage, personality, their ability to manage their disability or limitations in participation, redefinition of goals and ambitions and the disease trajectory (Taylor et al, 2008; Eiser and Jenney, 2007).

A search of the literature yielded no published data regarding the HRQoL of children with chronic conditions living in South Africa.

### **2.16 Measurement of Health Related Quality of Life**

HRQoL questionnaires are either generic or condition specific (Waters et al, 2009; Sawyer et al, 2004; Berzon, 1998, Osoba D, 1998). Generic tools offer the advantage of allowing comparisons between various populations of acute and chronic paediatric conditions as well as comparison between ill and healthy populations (Waters et al, 2009; Sawyer et al, 2004; Varni et al, 2002; Varni et al, 2001). The disadvantage of a generic HRQoL questionnaire is the potential inability to assess disease-specific factors that may affect HRQoL and treatment related changes that may occur (Waters et al, 2009; Sawyer et al, 2004; Eiser and Morse, 2001). The domains used to measure HRQoL in a generic measurement tool will differ to those used in a disease – specific measurement tool (Waters et al, 2009)

When choosing a questionnaire several factors must be taken into account namely: age, gender, educational level and degree of illness (Garvie et al 2009; Berzon, 1998). The level of cognitive development in children will influence their ability to use rating scales and understand and complete lengthy questionnaires that are often used in adult QoL assessments (Eiser and Morse, 2001). In children with HIV/AIDS, disclosure or non- disclosure will influence the choice of

using a disease specific measurement tool or a generic measurement tool (Garvie et al 2009). Inadvertent disclosure by medical staff needs to be avoided.

The purpose of measuring HRQoL will also dictate the type and length of questionnaire chosen. When screening a large group of individuals to identify possible domains of interest for future study and intervention, a brief measurement tool is used (Osoba, 1998). The advantages of using a brief measurement tool are two- fold: the ability to recruit large numbers of individuals into the study and minimal training is required of the interviewer (Eiser and Morse, 2001). The length of a questionnaire was not discussed in the literature however the recommended time span that a questionnaire should require for completion is 10- 20 minutes (Waters et al, 2009). For clinical trials and policy decision making, a more detailed measurement tool is required (Osoba, 1998).

The ability for children to self-report on their own quality of life has been debated in the literature. Developmental considerations which may hamper self-report include limited expressive and receptive language skills; the ability to interpret Likert scales; and the inability to understand time frames which involves memory and time perception ( Wallender et al, 2001). There is evidence however to show that children, as young as five years old, are reliable reporters of their own HRQoL (Varni et al, 2007) and child report is essential in measuring HRQoL (Varni et al, 2007). It is no longer acceptable to rely purely on parent proxy reports concerning their children's HRQoL (Eiser and Jenney, 2007; Cremeens et al, 2006; Sawyer et al, 2004; Varni et al, 1999).

## **2.17 Measurement Tools**

Two measurement tools were utilized in the research by the author. Both will be discussed below.

### **2.17.1 PedsQL 4.0 Generic Core Scale**

In reviews of measurement tools, both generic and disease specific, previously used for children/adolescents living with HIV/AIDS, no one tool proved ideal (Garvie et al, 2009; Clayson et al, 2006). Measuring HRQoL is unlike measuring other health indicators which provide empirical data; it is based on subjective opinion which is influenced by an endless array of external factors (Eiser and Morse, 2001). The PedsQL 4.0 Generic Core Scales has been found to be a valid and acceptable to measure HRQoL in HIV-infected children. It is able to distinguish between aspects of HRQoL in infected children and their uninfected counterparts (Banerjee et al, 2010).

The PedsQL 4.0 Generic Core Scales (Paediatric Quality of Life Inventory) is a brief, standardised generic assessment instrument that systematically assesses patients' and parents' perceptions of HRQoL in paediatric patients with chronic health conditions (Varni et al, 1999). The measurement tool is designed to measure the core health dimensions delineated by the WHO namely- physical functioning (eight items), emotional functioning (five items), social (five items) and school functioning (five items) (Varni et al, 2001). The generic version of the PedsQL was designed using paediatric cancer as the model (Varni et al, 1999). The PedsQL 4.0 Generic Core Scales are comprised of parallel child self-report for ages five-18 and parent proxy- report for ages two -18. (Varni et al, 2006). The necessity of using child self-reporting in measuring QoL has been stressed in the literature (Rosenbaum, 2008; Eiser and Morse, 2001).

The PedsQL 4.0 Generic Core Scale, self- report, for five- seven year old children was utilised in the research (Appendix I). The questionnaire is based on a three- point Likert scale with 0 (Never); 2 (Sometimes) and 4 (A Lot). Scores are transformed, using reverse scoring, on a scale of zero- 100. The domains are calculated separately as well as a total for all the domains is obtained. In addition a total for psychosocial functioning is obtained by combining the social functioning, emotional functioning and school functioning domains (Appendix II).

For the purpose of this research, the PedsQL Generic Core Scales has proved to be the measurement tool of choice due to the following factors:

- The PedsQL 4.0 Generic Core Scales child self-report, children ages five – 18, has been shown to demonstrate internal reliability as determined by calculating Cronbach's co-efficient alpha. For the Total Scale Score (child report),  $\alpha = 0.88$ . Construct validity was determined using the known-groups' method. When using this method, scale scores across groups known to differ in the health construct being tested are compared. The PedsQL 4.0 Generic Core Scales was found to be valid (Eiser and Morse, 2001; Janssens et al, 2008; Varni et al, 2007). Test – retest reliability for the PedsQL 4.0 Generic Core Scales, using ICC, Pearson correlation coefficients, and kappa, all exceeded the 0.60 level (Janssens et al, 2008)
- The PedsQL 4.0 Generic Core Scales has been found to be of the appropriate length for completion by children (Eiser and Morse, 2001).
- It covers many domains in the International Classification of Functioning, Disability and Health (ICF) (Janssens et al, 2008).
- In a study conducted by Varni et al (2002) the PedsQL 4.0 Generic Core Scale, has been shown to display sensitivity when assessing quality of life of children attending an orthopaedic out-patient clinic for treatment of fractures.

### **2.17.2 International Classification of Functioning, Disability and Health**

The International Classification of Functioning, Disability and Health (ICF) was introduced in 2001 (Simeonsson et al, 2006). The child and youth version (ICF-CY) was later introduced to improve coverage from birth to age 17. The ICF-CY offers a framework and common terminology to identify and research problems associated with body structures and functioning, activity limitations and participation restrictions. Influencing external factors, both positive and negative are also included. In terms of the PedsQL 4.0 Generic Core Scale, it has been found to cover the domains of activity limitation and participation in the ICF-CY (Janssens et al, 2008). The effects of a chronic disease on the HRQoL of a child

would be evident in the activity limitations and participation experienced by the child.

### **2.17.3 Household Economic and Social Status Inventory**

It has emerged that measuring socioeconomic status should not rely purely on self-reported income (Barbarin and Khoma, 1997). The use of self-reported income as a poverty measure proves problematic due to inaccurate reporting (Barbarin and Khoma, 1997). For the purposes of this research the Household Economic and Social Status Inventory (HESSI) was utilized to assess the socioeconomic status of the study and control group (APPENDIX III). Following their research between 1990 and 1996 on a cohort from Soweto, South Africa, Barbarin and Khoma (1997), were able to develop an instrument to measure material and social welfare that is sensitive to and reflects the variations within urban poor people. The instrument comprises various indicators that “reflect the economic and social circumstances characterizing the child-rearing environment among the poor” (Barbarin and Khoma, 1997).

### **2.18 Health Related Quality of life of Children infected with HIV**

The pre-ceding chapters dealing with HIV have drawn a clear picture of the many direct and indirect ways that HIV might impact on the quality of life of an individual. There has been a rapid increase in interest and research into measurement tools for HRQoL in adult patients with HIV/AIDS (Garvie, 2009; Clayson et al, 2006; Berzon and Lenderking, 1998; Shumaker and Naughton, 1997; Hays and Shapiro, 1992). However research into measurement tools used to measure HRQoL in children with HIV/AIDS has not been increasing at the same rate (Garvie et al, 2009). Since the commercial availability of HAART, no new measure of HRQoL for youth with HIV/AIDS has been established and validated (Garvie, 2009).

Researchers have used HRQoL as one of their outcomes to monitor and assess efficacy of HAART regimes (Lee et al, 2006; Storm et al, 2005) but few have

used HRQoL as the focal aim of their research (Banerjee et al, 2010; Bomba et al, 2010; Xu et al 2010; Oberdorfer et al, 2008).

There is research using children infected with HIV (Banerjee et al, 2010; Bomba et al, 2010; Xu et al 2010; Oberdorfer et al, 2008) and research using children affected by HIV ( have at least one infected parent) but not infected themselves (Xu et al, 2010). Thirdly there is a body of literature based on orphans and vulnerable children affected by HIV but without specific indication of the HIV status of the child (King et al, 2009; Richter, 2004). The term “orphans and vulnerable children” was first conceptualised by Foster and Williams in 2000 (Earls et al, 2008). Most of the research looking at the psychosocial effects of HIV/AIDS on children utilises these concepts. Skinner (2006) uses the definition of an orphan as a child younger than 18, who has lost either one parent (mother or father) or both parents (double orphan). UNICEF refers to maternal orphans, paternal orphans and double orphans (UNICEF, 2004). The definition of “vulnerability” has proven to be more culturally sensitive and diverse between countries, with no consistent definition emerging. In South Africa children are who are disabled, seen to be neglected, destitute or abandoned, living with terminally ill parents, born to single mothers, living with an unemployed caretakers, or who are abused or ill-treated by care-takers have all been identified as being vulnerable ( Skinner, 2006).

An analysis of research projects looking at HRQoL as the central outcome measure has shown that it is not only the positive HIV status of a child that will predict a lower quality of life but also living in a household affected by HIV. Xu et al (2010), using the PedsQL 4.0 Generic Core Scales, aimed to identify factors affecting the HRQoL of children affected by HIV. Of note is that only uninfected children living in a household affected by HIV were eligible for the study group. An affected household was considered to be one in which there was at least one HIV-infected parent or one or both were deceased due to HIV. A suitable control group of unaffected neighboring families was chosen. Children in affected



households reported significantly lower quality of life scores. HRQoL, as reported by the child, was found to be negatively affected by poor levels of self-esteem, caregivers' decreased QoL, and disclosure of parent's positive HIV status. Contrary to most research, a child experienced a better QoL when the caregiver was a grandparent.

In research carried out in Thailand, Oberdorfer et al (2008) found a direct relationship between reported QOL and CD4 percentage. Children with a CD4 count higher than 25% were reported to have a significantly higher QOL as compared to children with a CD4 count less than 25%. This research was based on parent-report and no control group was used. Without the use of a control group, values cannot be compared for uninfected children and no normal data and values, specific to Thailand are obtained. Very little data was available on exclusion and inclusion criteria of the children used in this research. Measurement tool used in the research was the General Health Assessment for Children developed by the Pediatric AIDS Clinical Trial Group (ACTG).

Using the PedsQL 4.0 Generic core Scales, Bomba et al (2010) and Banerjee et al (2010), were able to demonstrate a significant difference in the HRQoL of HIV-infected children as compared to a control group. Bomba et al (2010) used a sample of healthy randomly selected matched children whereas Banerjee et al (2010) used uninfected siblings and randomly selected healthy institutionalized children. Domains of physical functioning, emotional functioning and school functioning were affected in HIV-infected children in both studies. Limitations in Bomba et al (2010) included the limited number of children (27 in each group), and a large age-range (five-18 years of age) reflecting children in various stages of development which might affect perceptions of HRQoL and limited demographic data on subjects available.

It is difficult to compare data and results from all four research projects as different research tools, samples and methods were used. However certain

conclusions can be drawn concerning the HRQoL in HIV-infected children. HIV is a fluctuating chronic disease and therefore HRQoL would need to be assessed on a continuous basis thereby ensuring adequate and appropriate interventions. Despite the introduction and widespread use of HAART, HRQoL in HIV-infected children is still affected and children may require intervention.

## **2.19 Conclusion**

HIV/AIDS remains a chronic medical condition without a cure. It is a disease that affects all spheres of a child's life and their potential to participate in their family, social group and community. Continuous assessment of their HRQoL can perhaps help institute interventions that might help mitigate the negative effects of HIV/AIDS. The research describing and analyzing the HRQoL of the young HIV-infected child is limited, and requires more investigation. The PedsQL 4.0 Generic Core Scale has been found to be an appropriate measurement tool to analyze HRQoL in children infected with HIV.

## **Chapter 3: Methodology**

In this chapter the methodology used in this research report will be presented. This is a cross- sectional study.

### **3.1 Location of study**

This study was carried out at Charlotte Maxeke Johannesburg Academic Hospital and Chris Hani Baragwanath Hospital. Both hospitals are government run institutions and are situated in Johannesburg, South Africa. The study group was obtained from the Harriet Shezi Children's HIV clinic at Chris Hani Baragwanath Hospital and the paediatric HIV out-patient clinic at Charlotte Maxeke Academic Hospital. The comparison group of children was obtained from the paediatric orthopaedic out-patient clinics at each of the above hospitals and the paediatric out-patient dermatology clinic at the Charlotte Maxeke Academic Hospital.

### **3.2 Ethical Clearance**

Prior to commencement of data collection, ethical clearance was obtained from the University of the Witwatersrand Human Research Ethics Committee (Clearance number: R14/49 Goldberg, protocol number M081131) (Appendix IV). Further permission, in writing, was obtained from the respective hospitals to conduct the research. At each of the out-patient clinics, the research was discussed with the managing doctor and approved. Written informed consent was obtained from all caregivers and children participating in the research (Appendix V). To maintain privacy, no names were used in the research, with each child been identified by a number only.

### **3.3 The Study Population**

The data from 89 children, and their respective care-givers, who fulfilled the inclusion and exclusion criteria, was analyzed. The children in both groups resided in Soweto, Alexandra and Hillbrow, thus all coming from similar socio-economic backgrounds.

### **3.4 Sample Selection**

#### **3.4.1 Study group**

The data was collected from 45 consecutive children, aged six or seven, and their caregivers attending the respective HIV out-patient clinics. All 45 children had a confirmed diagnosis of HIV and were receiving treatment at the clinics on a regular basis.

#### **Inclusion criteria**

- Children with a CD4 count  $\geq 25\%$  were included in the study group.
- Children on HAART for a minimum duration of three months and longer. No specific regime of HAART was required.

#### **Exclusion criteria**

- Children in the study group who had any other chronic condition e.g. juvenile rheumatoid arthritis, haemophilia, active tuberculosis.
- Children presenting with clinical signs of physical and mental impairments that would impact on their quality of life.
- Children with severe physical and sensory deficits that render them unable to complete the PedsQL 4.0 Core Scale.
- Children who had been on antiretroviral therapy for less than three months.
- Children in the study group naive to HAART.
- Children living in an institution or foster care.
- Any children brought to the clinic by a family member unaware of the child's HIV status

### **3.4.2 Comparison group**

The comparison group was a sample of convenience. The data was collected from 44 children, aged six or seven, and their caregivers attending the respective clinics.

#### **Inclusion criteria**

- Children aged six or seven
- Attending only the orthopaedic out-patient clinic or dermatology out-patient clinic respectively.

#### **Exclusion Criteria**

- Any children in the comparison group who had previously been diagnosed with HIV/AIDS on admission to hospital or after discharge
- Children with any pre-existing diagnosed chronic condition that requires regular monthly clinic visits, and numerous days away from school every month.
- Children with extensive atopic dermatitis which may impact on their physical and emotional functioning.
- Children with multiple orthopaedic injuries that may impact on level of physical functioning or quality of life
- Children requiring any assistive devices for mobility or school function.
- Children in the comparison group requiring further orthopaedic management or interventions
- Children who reside in institutional care or foster-care.
- Children with severe physical and sensory deficits that rendered them unable to complete the PedsQL 4.0 Core Scale.
- Children from different socio-economic background.

### **3.5 Assessment tools**

The PedsQL 4.0 Generic Core Scales Child report for children aged five-seven was used. The measurement tool was used with permission from the author and the Mapi Research Trust. This tool was devised to measure the HRQoL in children aged 2-18 years and covers the domains of social, emotional, physical and school functioning. The length of time to administer the test is approximately 15 minutes.

The Household Economic and Social Status Inventory (HESSI) were used to collect socio-economic data. This is a tool that was developed in Soweto and has been used extensively in research in South Africa (Barbarin 1997; Potterton, 2007).

Additional information gathered from the patients' files included: CD4+ percentages, viral load status at time of research and the duration of HAART. For both groups of children, height and weight were measured.

### **3.6 Procedure**

#### **3.6.1 Translation of PedQL4.0 Generic Core Scale**

The PedsQL 4.0 Generic Core Scales was translated into Zulu using the translation agreement and procedure specified by the author and Mapi Research Trust. This procedure involved two independent translations of the PedsQL 4.0 Generic Core Scale edited into a final document. Back translations were required and reports of the procedure had to be submitted to the Mapi Research Trust. As per the agreement, both the child self-report and parent proxy report, for children aged five to seven, were translated. In this research however only the child self-report questionnaire was utilised. To ascertain the cognitive reliability of the translated PedsQL 4.0 Generic Core Scale, for children aged five-seven, the questionnaire was administered to five children and caregivers. The results were analysed and a report written to the author of the questionnaire and Mapi

Research Trust. Permission was then granted to use the questionnaire. Certain terminology in the document required altering, with agreement by the author, to enable a more accurate Zulu translation. ( APPENDIX VI)

### **3.6.2 Study Group**

Data was collected from 45 children aged six or seven years attending the HIV out-patient clinics at Charlotte Maxeke Academic Hospital and Harriet Shezi Clinic at Chris Hani Baragwanath Hospital. Prior to commencement of study a research assistant was trained to administer the measurement tool. The research assistant was able to communicate in various South African languages and English. Questionnaires were administered by the research assistant, with the principle researcher present at all interviews. As required by the translation agreement set out by Mapi Research Trust and the Author of the PedQL 4.0 Generic Core Scales, the questionnaire was piloted on five suitable children and caregivers. A report of the results was submitted for their approval. The questionnaires have been included

For the study group, suitable children were chosen by gathering the appropriate information from the file regarding the age, CD4+ percentage, viral load and duration of HAART. Caregivers were approached and informed about the nature of the research and the lack of disclosure involved. Informed consent was obtained from caregiver and assent was obtained from the child. All interviews were carried out in private with only the caregiver, child, research assistant and principle researcher present. The PedQL 4.0 Generic Core Scale child-report was administered to the child in a language understood by the caregiver and child. The questionnaire was administered as per requirements stated in the user agreement. As per exclusion criteria, if the child was unable to complete the questionnaire due to a lack of understanding or cognitive impairment, the child was excluded.

Additional information gathered included the weight and height of the child. The weight of each child was measured using the same scale (measured in kilograms) and the height was measured using the same measuring tape and method (measured in centimeters). The height was obtained by the child standing, without shoes, against a wall and measured from top of head to the floor.

Socioeconomic information gathered from the caregiver encompassed marital status, highest educational level achieved, employment, nature of housing, access to social grants, and the ownership of various household possessions.

### **3.6.3 Comparison group**

The above procedure was followed in obtaining children from the Orthopaedic out-patient clinics at Charlotte Maxeke Academic Hospital and Chris Hani Baragwanath Hospitals respectively. In addition children were also selected from the out-patient dermatology clinic at Charlotte Maxeke Academic Hospitals. Other clinics were not utilized so as to avoid selecting children with chronic diseases/conditions that could severely impact on their HRQoL. A total of 44 children were recruited into the comparison group. So as to further exclude children with chronic medical conditions, outpatient files and appointment records were checked, with caregiver consent, for history of hospital visits. Children in the comparison group were not required to undergo HIV testing nor were the caregivers questioned regarding the HIV status of the child. However if appointments for HIV outpatient clinics were noted in the out-patient records, the child was not selected.

Questionnaire administration, data collection and analysis followed the same procedure as for the study group.



### **3.7 Sample Size**

A sample size of 40 children in each group will have 90% power to detect a difference in mean scores in the PedsQL 4.0 Generic Core Scale, between children with HIV and comparison group, of 10.00, assuming that the common standard deviation is 15.00 using a two-group t-test with a 0.05 one-sided significance level (Dixon and Massey, 1983; O'Brien and Muller, 1983). A final sample of 45 children with HIV was selected and 44 children in the comparison group.

### **3.8 Statistical Analysis**

Various statistical tests were utilized in the analysis of the data. Fischer's exact test was used to analyze the demographic data. Fishers exact test was appropriate to use in the 2x2 tables with very small expected frequencies (Machin et al, 2007). Each domain total (Physical Functioning, Emotional Functioning, Social Functioning, School Functioning) was analyzed separately using Welsch-t test. The Welsch-t test is appropriate to use for two samples with possible unequal variances. Further analysis of all the domains as a single vector was done using Hotelling T<sup>2</sup>-test. This is used to compare means from two populations. In order to establish any covariants to the domains of the PedQL4.0 Generic Core scales, Anova test was done.

## **Chapter 4: RESULTS**

In chapter 4, the results of the study will be presented.

### **4.1 Demographics**

#### **4.1.1 Gender Distribution**

The gender distribution of the subjects participating in this study is shown in the table below

**Table 4.1 Gender distribution**

	<b>HIV Positive Group (n=45)</b>	<b>Comparison (n=44)</b>
<b>Female</b>	21 (46.67%)	19 (43.18%)
<b>Male</b>	24 (53.33%)	25 (56.82%)

(p = 0.83)

Eighty- nine children, 45 with a confirmed HIV diagnosis and 44 children in a comparison group were systematically questioned during the study period. Both groups were well matched for gender with no significant difference noted between the two groups (p= 0.83). The researcher did not set out intentionally to match gender, the above gender distribution was achieved randomly and unintentionally.

#### **4.1.2 Age Distribution**

The age distribution of the subjects participating in this study is shown in the table below.

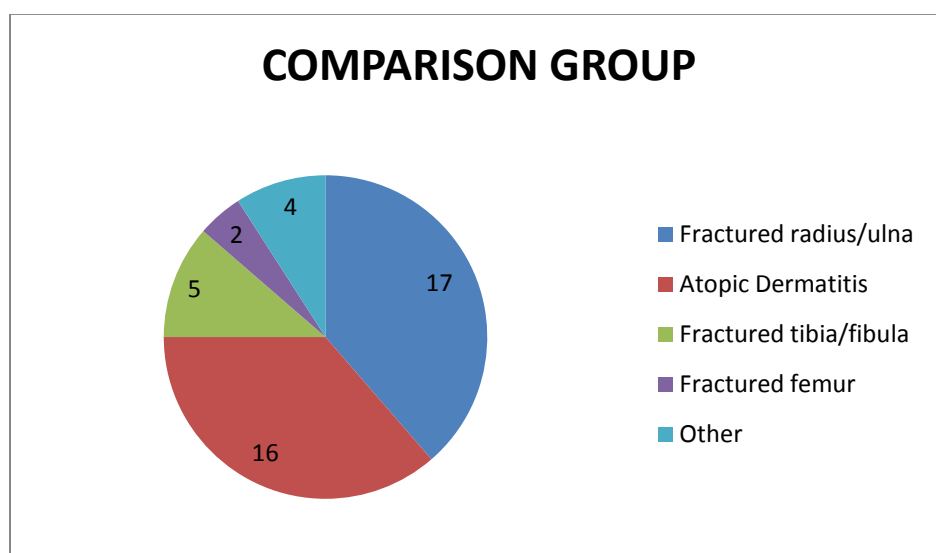
**Table 4.2 Age Distribution of the Sample**

	Positive	Comparison	p -value
Mean Age (sd) (95% cit.)	6.93 ( $\pm 0.5$ ) (6.75 ; 7.10)	6.74 ( $\pm 0.5$ ) (6.58 ; 6.90)	0.12

All the children in the study were aged six or seven. Using a Two-Sample t-test with equal variances no statistical difference was seen in the average age in each group. The mean age in the study group was 6.93 years and 6.74 years in the comparison group ( $p=0.12$ ).

#### 4.1.3 Composition of Comparison group

The comparison group was obtained from the orthopaedic and dermatology out-patient clinics. Children chosen to participate in the comparison group were diagnosed with either atopic dermatitis or a fractured lower limb or an upper limb.

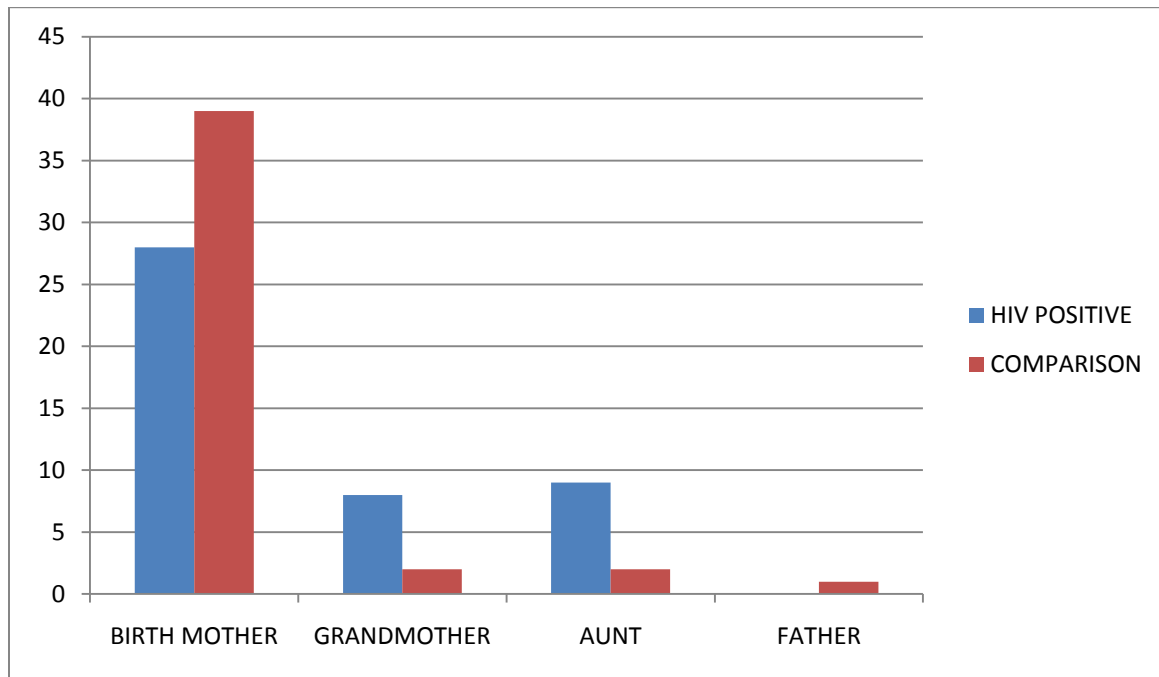


**Fig: 4.1 Composition of the comparison group by diagnosis and number**

#### 4.2 Socioeconomic Environment

Socioeconomic data was collected from the primary caregivers in both groups regarding the household environment in which the children reside.

### 4.2.1 Caregiver Relationship and Distribution



**Fig 4.2: Caregiver distribution of sample by number**

A significant difference was noted between the two groups with respect to primary caregiver of the child. In the study group only 28 (62.22%) as opposed to 39 (88.64%) children in the comparison group had their mother as the primary caregiver ( $p=0.01$ ). The children in the study group were more likely to have a grandmother (17.78%) or an aunt (20%) as the primary caregiver than in the comparison group 2(4.55%) and 2(4.55%) respectively. There were no significant differences noted in the marital status of the primary caregiver ( $p = 0.51$ ). The adult escorting the child on the day of assessment was not automatically deemed to be the primary caregiver. The primary caregiver was ascertained as the person primarily looking after the child, responsible for the welfare of the child and the person responsible for medical decision making for the child.

### 4.2.2 Caregiver Education Level

The table below indicates the highest education level obtained by the caregivers of the subjects participating in the study.

**Table 4.3 Educational Level of Caregiver**

<b>Education level</b>	<b>HIV Group (n=43)</b>	<b>Comparison group (n=42)</b>
<b>≤grade 11</b>	26 60.47%	14 33.33%
<b>Grade 12</b>	16 (37.21%)	16 (38.10%)
<b>Tertiary educ.</b>	1 (2.33%)	12 (28.57%)

(p=0.001)

A significant difference between the highest levels of education of caregiver was found between the two groups. It is evident that in the study group the majority of caregivers are distributed between the lower two categories. In contrast, the caregivers in the comparison group are distributed in the upper two categories with as many as 28.57% reaching level of tertiary education. For four of the participants (two in each group), information regarding the highest educational level of the caregiver was unavailable.

#### **4.2.3 Employment status of caregiver and Care Dependency Grants**

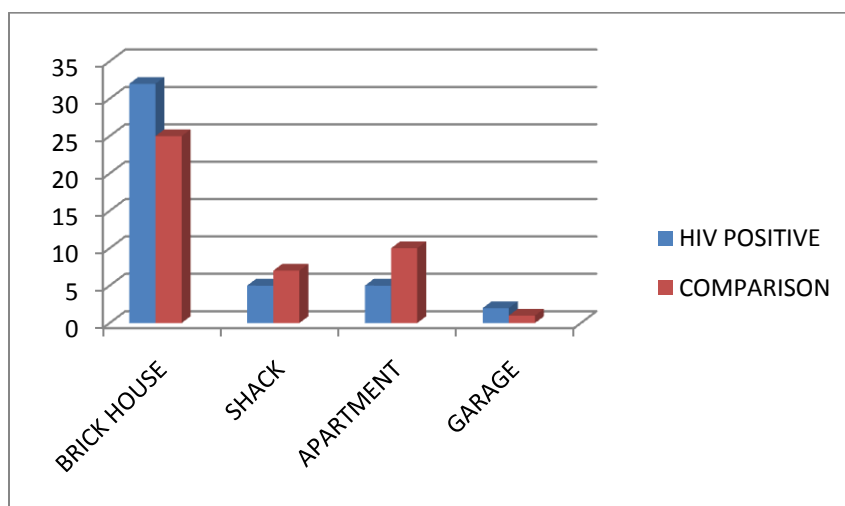
The results show that even though there is no significant difference in the employment rate of the care-givers in the study group ( $p = 0.28$ ), there is however a significant difference between the number of children who receive social support grants - with 75% of HIV positive children receiving grants as opposed to only 53.49% of the comparison group receiving grants ( $p = 0.05$ ). The grants received refer to Care Dependency grants and not Disability grants.

**Table 4.4 Employment status of primary caregiver and care dependency grant**

	HIV positive (n=44)	Comparison (n=43)	p value
Caregiver employed	22 (50%)	27(62.79%)	0.28
Care Dep. Grant received	33 (75%)	23 (53.49%)	0.04

#### 4.2.4 Housing

From the HESSI questionnaire, the researcher was able to establish that there were four types of dwellings that were the most common and, using Fisher's exact test, showed no significant difference in the two groups. The most common form of housing in both groups was the stand alone brick house (56%). The shacks seen in the informal settlements accounted for 12% and apartments 15% for the total. There were 3 children reported to be living in a single garage structure.



**Fig 4.3 Type of Housing by number**

Other items measured in the HESSI indicating economic standard showed no significant differences between the two groups. These items include the possession a television, DVD machine, cell phone, washing machine, microwave and a motorcar.

### 4.3 Anthropometric Analysis (Height, Weight and BMI)

The table below illustrates the differences in height and weight of the subjects participating in the study. The weight is measured in kilograms and the height in centimetres.

**Table 4.5 Growth Parameters of children**

<b>Growth Parameters</b>	<b>HIV Positive n= 43</b>	<b>Comparison n=44</b>	<b>Welch T-Test p-Value</b>
<b>Height Mean (sd) (95% ci)</b>	113.3 (6.3) (111.4 ; 115.2)	119.9 (5.7) (118.1 ; 121.6)	p < 0 .01
<b>Weight Mean (sd) (95%ci)</b>	20.3 (3.0) (19.4 ; 21.2)	22.8 (4.7) (21.4 ; 24.3)	p< 0.01
<b>BMI Mean (sd) (95%ci)</b>	15.6 (1.6) (15.1 ; 16.1)	15.8 (2.5) (15.0 ; 16.5)	p=0.75

The above results indicate that despite significant difference in height ( $p<0.01$ ) and weight ( $p<0.01$ ) between the children in the study and comparison groups, the BMI of the children are not significantly different ( $p=0.75$ ). This indicates that their weight and height are in proportion. The WHO-Multicentre Growth Reference Study Standards were not utilised as the data for height and weight was not analysed by sex but rather as a mean for each group. Data regarding height and weight of two children in the study group was not measured.

### 4.4 Analysis of the PedsQL 4.0 Generic Core Scale Results

The PedsQL 4.0 Generic Core Scale child-report consists of 23 equally weighted questions separated into four domains (physical functioning, social functioning,

emotional functioning and school functioning). A better HRQoL is associated with a higher score. If more than 50% of the questions in a domain are not answered, that domain cannot be calculated. If more than 50% of the entire questionnaire is unanswered, the scale cannot be calculated. All the participants completed the questionnaire.

**Table 4.6 PedsQL Results**

<b>PedsQL Domain</b>	<b>HIV (n=45) Mean (sd) (95% CI)</b>	<b>Comparison (n=44) Mean (sd) (95% CI)</b>	<b>HotellingT<sup>2</sup> test p-value</b>	<b>Welch t- test p- value</b>
<b>PF</b>	71.4 (23.6) (64.3 ;78.5)	86.8 (11.6) (83.3 ; 90.4)	p<0.01	p<0.01
<b>EF</b>	74.3 (21.3) (67.9 ; 80.7)	82.5 (15.6) (77.9 ; 87.2)		p=0.04
<b>SF</b>	77.3 (22.2) (70.7 ; 84.0)	88.7 (13.5) (84.5 ; 92.8)		p<0.01
<b>SCF</b>	71.6 (20.2) (65.6 ; 77.6)	79.5 (14.9) (75.0 ; 84.0)		p=0.04
<b>EF+SF+SCF (Psychosoc)</b>	73.9 (17.7) (68.6 ; 79.2)	83.6 (10.6) (80.4 ; 86.8)		p<0.01
<b>Total Score</b>	73.8 (14.9) (69.3 ; 78.3)	84.7 (8.9) (82.0 ; 87.4)		p<0.01

PF= physical Functioning; EF=Emotional Functioning; SF= Social Functioning; SCF=School Functioning; Psychosocial = emotional+ social+ school functioning



With respect to the PedQL domain vector (PF, EF, SF, SCF) the HIV and comparison groups differed significantly ( $p=0.0018$ ), in particular, significant differences were detected for each of the domains using Welch t-test ( $p<0.01$ ;  $p=0.04$ ;  $p<0.01$ ;  $p=0.04$ ). Controls had higher scores in all domains and in total score. From the data, it appears that the physical functioning of the children infected with HIV displays the greatest disparity as compared to the children in the comparison group. When controlling for the possible co-variants Care-giver relationship, care-giver education level and social grant, only for Physical Functioning caregiver relationship was a significant co-variant and after adjusting for this, ( $p<0.01$ )

#### **4.5 Analysis of HRQoL, CD4+, Duration of HAART Treatment and Viral load**

Using a Regression Analysis and plotting of data, no relationship could be established between the total scores obtained on the PedsQL 4.0 Generic Core Scale, CD4+ percentages and duration of HAART. The average percentage of CD4+ was 33.21%. In addition, due to the nature of reporting of viral load in patient files, the author was unable to analyse the effects of viral load on HRQoL. The nature of viral load reporting depended on the clinic where the child attended. It was reported as either  $< 25$  copies/mL or as having the “lowest detectable level” (LDL) as opposed to an actual viral load measure. The average duration of HAART treatment was 2.6 years.

#### **4.6 Summary of Findings**

In this research, the HRQoL of 89 children was evaluated. The children were divided into a study group (45 children known to be HIV positive) and a comparison group (44 children). Both groups were well matched for gender and age. Significant differences found between the two groups were with respect to the primary caregiver, highest educational level achieved by primary caregiver and care dependency grant status. Analysis of the height and weight of all the

children revealed a difference between the two groups, with the HIV-infected children being both significantly shorter and lighter than the comparison group.

The HRQoL, as measured by the PedQL4.0 Generic Core Scale child self-report (ages five-seven), indicated a significant difference between the two groups of children. The HIV-infected children were found to have a lower overall HRQoL with all four domains (Physical Functioning; Emotional Functioning; Social Functioning and School Functioning) showing significant differences. The domain of Physical Functioning showed the greatest difference between the two groups.

No relationship could be found between CD4+, duration of HAART treatment, viral loads and the reported HRQoL of the HIV-infected children. These results will be discussed in chapter five.

## **Chapter 5: DISCUSSION**

In chapter five the results obtained from the study will be discussed, and compared to data obtained from other relevant research pertaining to HRQoL and HIV. Furthermore the limitations of the study and recommendations for future studies will be discussed.

### **5.1 Demographics**

In this study the HRQoL of 89 children (45 known HIV- positive children and 44 control children) was evaluated, using the PedsQL 4.0 Generic Core Scale. Both groups were well matched for age (all children were either aged six or seven with  $p= 0.12$ ), and gender ( $p=0.83$ ). Previous studies using this assessment tool with children who are HIV positive have used children of a wider age range (Banerjee et al, 2010; Bomba et al, 2010) and smaller number of children (Bomba et al, 2010). By limiting the age range in this research, the influence of developmental and life stages (e.g. adolescence) on perceptions of HRQOL would be reduced. Adolescent children infected with HIV, face many challenges that would influence their perceptions of HRQoL (Mellins et al, 2004).

The cognitive and psychosocial effects of poor socio-economic status on child development are well documented (Chandan and Richter, 2009; Earls et al, 2008). Therefore it is imperative that in assessing quality of life, the effect of socio-economic status cannot be ignored. In order to limit the variations in socioeconomic status within the study and comparison groups, all the children assessed were chosen from two public hospitals namely Chris Hani Baragwanath and Charlotte Maxeke Academic Hospital, servicing children from areas traditionally associated with poor socio-economic backgrounds. All of the children, with the exception of one child, resided in the greater Soweto area, Alexandra and Hillbrow. None of the children had access to private medical care and were completely reliant on state care. There were no significant differences found in the rate of employment of caregiver, type of housing, sanitary facilities

and household items (television, DVD player, fridge, microwave, washing machine and motor vehicle).

There was however a significant difference noted between the two groups with respect to whether or not the children were receiving a care dependency grant ( $p=0.04$ ). The caregivers of HIV infected children were more likely to be receiving financial support from the government in the form of a care grant. This grant is not specifically aimed at HIV positive children but rather for all children (healthy or ill) being cared for in a poor economic environment; however caring for a child who is HIV positive is more costly to the caregiver (Petersen et al, 2010). In this research the primary caregiver was not necessarily the person accompanying the child to the clinic but rather the person primarily responsible for the child. The fact that more caregivers of HIV positive children require a care grant points to the vulnerability of the families and children. The socioeconomic impact of HIV on families has been discussed in the literature review. Further indicating the vulnerability of the children with HIV in the study group was the significant difference in highest education level of the caregiver in the study group ( $p<0.01$ ). The level of education of the primary caregiver has been associated with socioeconomic status (Varni et al, 2001).

The nature of the caregiver relationship, between the two groups, was found to be significantly different ( $p=0.01$ ). Children with HIV were less likely to be looked after by their biological mother as compared to the comparison group. This is easily explained by the nature of the disease and its progression to death if not treated. In this report it was found that only 62.22% of the children in the study group were primarily cared for by their biological mother. This was similar to Bomba et al (2010) where 63% of the HIV-infected children lived with their biological mother. The percentage of children in this current research, with their biological mother as the primary caregiver, differs significantly from Potterton et al (2009) who found that in their cohort, obtained from the same clinic at Chris Hani Baragwanath Hospital, the biological mother was the primary caregiver in

81% of the children. The significance arises from the age difference in the two groups. In Potterton et al (2009), the average age was 18 months, with all children younger than two and a half years. This shows that as the age of the HIV-infected children increases, the likelihood of them having become maternal-orphans increases. Richter (2004) estimates that between 20% and 30% of children affected by HIV, by the ages ten to 14 would have lost their biological mother if she was HIV positive. The consequences of this on the child are numerous with them being affected medically, financially, socially and psychologically (Desmond, 2009; Andrews, 2006).

## **5.2 Comparison group**

The comparison group was chosen as a sample of convenience from the paediatric out-patient orthopaedic clinics (Chris Hani Baragwanath Hospital and Charlotte Maxeke Academic Hospital) and the dermatology out-patient clinic (Charlotte Maxeke Clinic). The choice of using these children as opposed to a sample obtained from the community or a school setting was to try and eliminate the possibility of the children in the comparison group being HIV positive. For ethical reasons the children in the comparison group did not require HIV testing. To limit the possibility of HIV infection, hospital out-patient records in the caregivers' possession were checked, with consent, to establish any previous admissions and clinic visits that would point to the possibility of HIV infection. Strict admission criteria were followed to avoid the admission of children with other chronic diseases that would have influenced their reported HRQoL.

## **5.3 PedsQL 4.0 Generic Core Scales**

The PedsQL 4.0 Generic Core Scales has been found to be a valid and reliable HRQoL measurement tool in children with chronic diseases, school-going children (Varni et al, 2006; Varni et al, 2001; Eiser and Morse, 2000; Varni et al, 1999) and children infected with HIV (Banerjee, 2010). There is no consensus in the literature with regard to the most appropriate measurement tool to be used in HIV research (Clayson et al, 2006). The very nature of the disease with its

changing impact on the individual requires the varied use of measurement tools most appropriate for that stage. The PedsQL 4.0 Generic Core Scales proved ideal for the purposes of this research due to its validity, reliability, length and ease of administration, as well as the fact that the terms HIV and/or AIDS are not used, thereby avoiding inadvertent disclosure to the child. There was no prior knowledge on whether the child was aware of his/her positive HIV status. This often dictates the use of a generic HRQoL measurement tool and not a disease specific tool (Garvie et al, 2009). The objective of this research was not to analyse treatment or clinical outcomes thereby allowing for the use of a generic measurement tool as opposed to a disease specific measurement tool (Eiser and Morse, 2000).

The results from this research show that the children in the study group (with known HIV infection) scored significantly lower in all four domains of the PedsQL4.0 Generic Core Scale (Physical Functioning, Social Functioning, Emotional Functioning, School Functioning), with an overall total score significantly lower than the comparison group indicating a lower quality of life as compared to the comparison group ( $p < 0.01$ ). It has previously been shown, using the PedsQL 4.0 Generic Core Scale that children with chronic diseases score lower in all four domains with a subsequent lower reported quality of life (Varni et al, 2001). The mean scores of the HIV infected children in this research study group were lower than those reported by children with other chronic diseases as reported by Varni et al (2001). The specific chronic conditions were not indicated in Varni et al (2001). No research was found pertaining to the reported HRQoL of children with chronic medical conditions, other than HIV, in Africa.

In this research, the domain of physical functioning revealed the most significant difference between the study and comparison groups ( $p < 0.01$ ). This correlates with the results from Bomba et al (2010) conducted in Italy. The decrease in physical functioning could possibly be attributed to the known fact of growth stunting and weakness in children with HIV infection (Isanka, 2009; Potterton et

al, 2009; Storm, 2005; European Collaborative Study, 2003; Missmer et al, 2000). This marked differences in height and weight between the two groups was evident in this research ( $p<0.01$  and  $p=0.04$  respectively). When controlling for possible covariants for physical functioning, only care giver relationship was found to be a significant covariant ( $p<0.01$ ). Caregiver education level and grant status were not found to be significant covariants on the physical functioning. The reason for the influence of caregiver relationship on the physical functioning of the child remains unclear. The negative effect of HIV infection on the physical functioning of children has been demonstrated in other studies, using various other assessment tools (Lee et al, 2008; Oberdorfer et al, 2008; Missmer et al, 2000).

HIV-infected children scored significantly lower in the domains of Social, Emotional and School Functioning ( $p<0.01$ ;  $p=0.04$ ;  $p=0.04$  respectively). With respect to social functioning, this result differs to Banerjee et al (2010) where HIV-infected children scored higher scores in this domain as opposed to uninfected children. Bomba et al (2010) found no difference in social functioning between their two groups. Banerjee et al (2010) suggest that the better social functioning found in their HIV-infected children, could relate to the exposure to increased emotional and social interventions that are offered at the HIV clinics. The uninfected children were not afforded the opportunity to access such services in their communities.

Collectively, the Psychosocial Functioning (Emotional, Social and School Functioning combined) of the children with HIV infection proved significantly lower than those in the comparison group ( $p<0.01$ ). Children with chronic diseases have been shown to be more susceptible to psychosocial problems (Gannoni and Shute, 2010; Scharko et al, 2006). The possible factors that could be affecting the psychosocial functioning and overall lower reported HRQoL in this sample of HIV-infected children include: (1) limitations in physical functioning could affect the ability of the child to interact effectively with his/her peers; (2) living in a household affected by HIV has been shown to have a negative effect

on the psychosocial functioning of the child, even if the child is not HIV positive (Xu et al, 2010); (3) there was a significant difference in access to care grants ( $p=0.04$ ), with HIV-infected children more likely to be receiving social support, this would indicate an increased vulnerability of the families affected by HIV and the consequent socio-economic ramifications. This increased vulnerability may be contributing to the psychosocial functioning of the HIV-infected children. When controlling for possible covariants - caregiver relationship, caregiver education level and care grant status, proved not to be significant covariants with respect to Psychosocial Functioning.

The author was unable to compare results from the PedsQL 4.0 Generic Core Scale to other research conducted in South Africa. No other literature pertaining to HRQoL or QoL in South African children with chronic medical conditions was found. The only published data available is for QoL of children, using the PedsQL, in children post burns (Weedon and Potterton, 2011).

The disclosure status for the children was unknown and therefore the impact thereof and associated stigmatization on psychosocial functioning could not be assessed. In a previous study on HIV-positive adolescents in South Africa disclosure was associated with a withdrawal from previous social groups and activities (Petersen et al, 2010).

Analysis of the relationship of severity of disease (%CD4+) and duration of HAART on the HRQoL of the children with HIV (study group) yielded no significant pattern. This may be due to various factors including: (1) all of the children had a CD4+ count  $\geq 25\%$ , indicating no immune-suppression according to the CDC classification (Centre for Disease Control, 1994) with no consequent negative impact on HRQoL, (2) there was a very limited range of CD4+ percentages with little variation and hence a limited effect on HRQoL total scores obtained. With respect to HAART, there were only five children in the study group with duration of HAART of less than 12 months. The remainder of the children



had been receiving HAART for a mean of 35.4 months. With this duration of receiving HAART, there may be less number of side-effects that may still be impacting on HRQoL.

The impact of viral load on the HRQoL of the HIV-infected children could not be studied. In most cases an actual value for viral load was not recorded in the files, it was reported as “lowest detectable level”.

It is interesting to note that the children in the comparison group, despite the occurrence of a fracture or presence of a contact dermatitis, scored comparably, in all four domains, to a group of healthy children used by Varni et al (2001).

#### **5.4 Limitations of the research**

Limitations in research on HRQoL and QoL are inevitable (Eiser and Morse, 2001). With reference to this research, the following limitations were noted:

- The use of a generic HRQoL measurement tool does not allow for the evaluation of HRQoL with respect to the impact of a specific disease.
- Only the child self-report was carried out. The parent-proxy report was not performed.
- Comparison group did not undergo HIV testing, thereby allowing the possibility that some of the children could have been HIV positive despite not showing any signs of infection. However the children in the comparison group were asymptomatic with respect to signs and symptoms relating to HIV infection, nor were they on any chronic medication. The researcher hence does not feel that the results would have differed significantly if comparison group did undergo HIV testing.
- A very narrow age gap was used; therefore these findings may not be generalized to other age groups of children.

- The PedsQL 4.0 Generic Core Scale has not been validated and normed for healthy black South-African children.

### **5.5 Relevance to Clinical Practice and Recommendations Based on Results**

The group of HIV-positive Children aged six or seven, beginning their school career, reported a lower HRQoL than their peers attending orthopaedic or dermatology clinics. Scores in all four domains were significantly lower, indicating difficulties with physical and psychosocial functioning (social, emotional and school functioning). It is evident that services offered at paediatric HIV clinics should not only concentrate on medical management. With the introduction of HAART, and HIV becoming a chronic paediatric disease, it has become essential to treat the child holistically. The need for a multi-disciplinary approach, meeting the medical, social and psychological needs is essential and yet limited to only a few regions in the world (Earls et al, 2008). The results of this research indicate the need for psychologists, educational psychologists and allied health therapists to be involved in the daily care of these children. Ongoing intervention in all spheres of functioning may be necessary to ensure a smooth transition into adolescence. This intervention should not be based only at the clinics but should be extended into the community setting and school environment.

In addition programmes should be extended to the needs of the caregivers. It has been suggested that it is through effective programmes targeting the support of caregivers and strengthening the family (economically and psychologically) that the negative impact of HIV on children could be to a large extent lessened (Petersen et al, 2010; Chandan and Richter, 2009; Desmond, 2009). It has been suggested that all facilities dispensing HAART and treating children with HIV, should dedicate at least one day a week to family based intervention (Meyers et al, 2007).

### **5.6 Recommendations for Future Research**

This research has shown that HIV-infected children report a lower HRQoL.

- The creation of a reliable, valid, culturally sensitive and medically appropriate questionnaire, for sub-Saharan Africa, needs to be developed. The questionnaire should focus both on generic aspects of HRQoL as well as the disease specific effects on HRQoL.
- Correlation of HRQoL and viral load needs to be investigated in this paediatric HIV population.
- Research is required to evaluate the HRQoL of children with CD4+ percentages above 25% (indicating immune suppression). The intervention services they require might differ to those healthier children infected with HIV.
- A prospective study of HRQoL would be necessary to indicate the changes in HRQoL with children moving into adolescence and early adulthood as well as with disease progression.
- Research including a wider age range of children would be beneficial to assess the impact of stage of development on HRQoL.

## **Chapter 6: CONCLUSION**

In 2008, 1.8 million HIV-infected children were living in sub-Saharan Africa (UNAIDS Report, 2009). With the introduction of HAART, HIV has become a chronic illness (Garvie et al, 2009). HRQoL has become an important medical outcome to consider in children infected with HIV. The aim of this research was to evaluate the HRQoL of 89 children, aged six or seven, attending government run clinics. The PedQL4.0 Generic Core Scale, child self-report (ages 5-7) was used as the measurement tool. The children were divided into two groups, those known to be HIV positive (45) and a comparison group (44). Subjects were well matched for age and gender and all were from similar socioeconomic backgrounds.

The PedQL 4.0 Generic Core Scale has been used previously in research evaluating the HRQoL of children with HIV. The tool has been found to be reliable and valid. For the purposes of this research, the questionnaire was translated into Zulu as per translation instructions set out.

The results indicated that HIV-infected children reported a lower HRQoL as compared to a comparison group of children. Although all four domains (Physical, Emotional, Social and School Functioning) were affected, Physical Functioning of the HIV-infected children appeared to be the most compromised. This finding supports previous research which found similar findings with respect to physical functioning. No relationship could be established between HRQoL and CD4+ percentages, viral load or HAART duration. Children with HIV were found to be shorter and lighter than those in the comparison group. This corresponds to previous research in the literature.

There is a need for further research to determine the ongoing effect of HIV on the HRQoL of children living in South-Africa. Children of different ages and developmental capabilities need to be included in the research. This is essential

to establish effective interventions to maximize HRQoL which would facilitate the effective development of children into adolescents and adults who are able to interact effectively with their families, communities and society as a whole.

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## Appendix I

### PedsQL 4.0 Generic Core Scale, Child Self- Report

(Ages 5-7)

## Appendix II

### Scoring of PedsQL 4.0 Generic Core Scale

## Appendix III

### HESSI Questionnaire

## Appendix IV

### Ethical Clearance

**UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG**

Division of the Deputy Registrar (Research)

**HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)**

R14/49 Goldberg

**CLEARANCE CERTIFICATE**

**PROTOCOL NUMBER M081131**

**PROJECT**

An Evaluation of the Quality of Life  
of Children with human Immunodeficiency  
Virus/Acquired Immunodeficiency  
Syndrome

**INVESTIGATORS**

Mrs L Goldberg

**DEPARTMENT**

Physiotherapy Department

**DATE CONSIDERED**

08.11.28

**DECISION OF THE COMMITTEE\***

Approved unconditionally

**Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.**

**DATE** 09.01.30

**CHAIRPERSON** .....



(Professor P E Cleaton Jones)

\*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : J Potterton

**DECLARATION OF INVESTIGATOR(S)**

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.

I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...

## Appendix V

### Consent Forms



## **AN EVALUATION OF THE QUALITY OF LIFE OF CHILDREN WITH HIV/AIDS.**

### **INFORMATION SHEET FOR THE COMPARISON GROUP**

Dear Parent/ caregiver

Hello, my name is Linda Goldberg; I am a physiotherapist working at the Charlotte Maxeke Johannesburg Academic Hospital.

I am doing research to look at the quality of life of children aged six or seven currently attending Grade one.

If you agree to participate in the study, I will be asking your child to fill out a short questionnaire. The questionnaire is short and will take her fifteen minutes to fill in. The questions are short and easy to understand. The questions have been translated into Zulu and there is someone to assist you with the questions. In the questionnaire I will be asking her if she can walk, run, play, bathe herself and help in the house. Other questions will be about how she is feeling (sad, angry or worried about anything or having any pain). I will be asking her about her friends and how she plays with them, if it is hard to make friends. Finally I will be asking her how she is managing with her schoolwork.

I will also need to ask you a few questions about your household, and your child's health. This questionnaire will take you 5 minutes to complete. There are questions about the size of your family, the type of house you live in and your last year that you attended school. It will also ask about your income and if anyone is working. The questionnaire is in English but we can assist you.

In addition I will be asking your permission to look at your child's medical record to get information about her orthopaedic treatment in the hospital, her medicine and whether she attends any other clinics at the hospital. I will not be using your name or your child's name in the study so that your privacy will be kept at all times. At no time will your child

be asked to have any blood tests or painful procedures. The information I get from you will be compared to a separate group of children attending HIV/AIDS outpatient clinic at Baragwanath and Charlotte Maxeke Hospital.

This study is voluntary and only if you choose to participate you will be included. If at any time you choose not to continue in the study, you are free to withdraw. This will have no effect on the treatment you get at this clinic.

If you and your child would like to participate in this study please fill in the form below. If at any stage you have any questions about this research, please contact me on the number 082-5191447. Or you could contact Professor Cleaton-Jones at the Wits Ethics Committee at the number 011 717-1234.

Thank you so much

Linda Goldberg (physiotherapist)  
082 519 1447

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## CONSENT FORM

I \_\_\_\_\_ agree to participate in the study. My child,

\_\_\_\_\_ will also join the study.

I understand that we can withdraw from the study at any time.

Signed \_\_\_\_\_

Date \_\_\_\_\_

Researcher \_\_\_\_\_

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## **AN EVALUATION OF THE QUALITY OF LIFE OF CHILDREN WITH HIV/AIDS**

### **Children's' information sheet**

Hello, my name is Linda Goldberg. I am a physiotherapist. A physiotherapist is someone who works in the hospital with children.

Today I would like to ask you some questions about you. It will take 15 minutes to answer all the questions, but if you don't want me to ask you the questions – you don't have to. The questions I would like to ask you are about different things. The first thing I will be asking you about is how strong you are feeling. Do you find it hard to walk, run, play sports, take a bath and help around the home?

The next thing I will be asking you is about your feelings. Do you feel scared, sad, angry or worried about anything? Do you feel any pain anywhere on your body?

The third thing I will be asking you is about your friends. Do you have lots of friends, do you play nicely with them or do they tease you.

The last thing I will be asking you about is how you are enjoying school. Is it easy for you at school; is it hard to remember things?

If you would like to answer the questions, there is someone to help you with the questions and your mom can stay with you. Remember, there is nothing that you

have to do if you don't want to. While you are answering the questions, I will be looking at your file to get some information about you and your hospital visit. I will also have to ask the person you have come to the clinic with some questions about your house and the people looking after you.

If you choose not to answer the questions, no one will be cross with you. And if you choose to do some and then stop, that is ok.

Thank you so much

Linda Goldberg (physiotherapist)

## CHILD CONSENT FORM

I \_\_\_\_\_ would like to answer the questions.

Name \_\_\_\_\_

Date \_\_\_\_\_

Researcher \_\_\_\_\_

# **AN EVALUATION OF THE QUALITY OF LIFE OF CHILDREN WITH HIV/AIDS**

## **CONSENT FORM FOR STUDY GROUP**

Dear parent/ caregiver

Hello, my name is Linda Goldberg and I am a physiotherapist working at the Charlotte Maxeke Johannesburg Academic Hospital. I am doing research at this clinic looking at children who are six or seven years old and are in Grade 1 at school. I am trying to find out more about your child's quality of life. I would like to include your child in the study.

If you would like to participate in the study, I will be asking your child to fill out a short questionnaire. The questionnaire is short and will take her fifteen minutes to fill in. The questions are short and easy to understand. In the questionnaire I will be asking her if she can walk, run, play, bathe herself and help in the house. Other questions will be about how she is feeling (sad, angry or worried about anything). I will be asking her about her friends and how she plays with them, if it is hard to make friends. Finally I will be asking her how she is managing at work and with her schoolwork. Your child will only need to do the questionnaire once.

In addition, I am asking you for your permission to look in your child's medical file to get information on your child's latest CD4 count and length of time on antiretroviral medication. If your child has been on medication for less than 3 months, she will not be able to join the study.

I will also need to ask you a few questions about your household, your family and your child's health. This questionnaire will take you 5 minutes to complete. There are questions about the size of your family, the type of house you live in and the year you

finished school . It will also ask about your income and who is working in the family. The questionnaire is in English but we can assist you in translating.

Your child's name or your name will not be used in the study, making sure that your privacy is kept and there is no disclosure to anyone.

If at any time you choose not to continue with the study, you are free to do so. This will have no effect on the treatment you child will get at the clinic.

If you agree to take part in this study please complete the form below. If at any time you would like to ask me any questions, please feel free to contact me on 082-5191447. Or you can contact Professor Cleaton-Jones at the Wits Ethics Committee on the number 011 717-1234

Thank you so much for your help.

Linda Goldberg (physiotherapist)



**PARENT/CAREGIVER CONSENT**

I-\_\_\_\_\_agree that I and my child\_\_\_\_\_

Will join this study. I understand that we can withdraw from the study at any time.

Signed\_\_\_\_\_

Date\_\_\_\_\_

Researcher\_\_\_\_\_

\_\_\_\_\_

## Appendix VI

### Zulu Translation of PedsQL 4.0 Generic Core Scale, Child Self- Report (Ages 5-7)

ID#:	_____
Usuku:	_____

# PedsQL™

## Uhlu lwemibuzo ngezininga lempilo yezingane

Ihlelo 4.0

### UMBIKO WENGANE ENCANE (iminyaka yobudala eyi-5 kuya kweyi-7)

Imiyalelo yomuntu obuza imibuzo:

***Ngizokubuza eminye imibuzo ngezinto ezingaba inkinga kwezinye izingane. Ngifuna ukwazi ukuthi lezi zinto zingaba inkinga kangakanani kuwe.***




Khombisa ingane uhlaka (template) bese ukhomba izimpendulo lapho ufunda.

***Uma kungesiyo nhlobo inkinga kuwe, khomba ubuso obumamathekayo.***

***Uma kuyinkinga ngezinye izikhathi, khomba ubuso obuphakathi nendawo.***

***Uma kuyinkinga kuwe kakhulu, khomba ubuso obuphatheke kabi.***

***Ngizofunda umbuzo ngamunye. Khomba ezithombeni ukungibonisa ukuthi kuyinkinga kangakanani kuwe. Ake sizame ukukwenza kuqala sibone ukuthi kuzokwenzeka yini.***

	Akusiyo Nhlobo	Ngezinye izikhathi	Kakhulu
Kuyinkinga kuwe <i>ukucwayiza</i>			

Cela ingane ukuthi ikhombise ukucwayiza ukuze ubone ukuthi umbuzo uphendulwe kahle yini. Uphinde umbuzo uma ingane ikhombisa impendulo ehluke kulokhu ekwenzayo.

***Cabanga ngokuthi ubunjani emasontweni ambalwa edlule. Ngicela ulalele umusho ngamunye ngokucophelela bese ungitshele ukuthi kuyinkinga kangakanani lokhu kuwe.***

Emva kokufunda into, khomba ohlakeni. Uma ingane ingabaza noma ingaqondi ukuthi kufanele iphendule kanjani, funda ukhetho lwezimpendulo ngesikhathi ukhomba ubuso

<b>Impilo Yakho (izinkinga ...)</b>	<b>Akuyis o Nhlobo</b>	<b>Ngezinye izikhathi</b>	<b>kakhulu</b>
1. Ngabe kunzima ukuthi uhambe	0	2	4
2. Ngabe kunzima ukuthi ugijime	0	2	4
3. Ngabe kunzima ukuthi udlale imidlalo noma uvocavoce umzimba	0	2	4
4. Ngabe kunzima ukuthi uphakamise izinto ezinkulu	0	2	4
5. Ngabe kunzima ukuthi ugeze ebhavini noma eshaweni	0	2	4
6. Ngabe kunzima ukuthi wenze imisebenzi yasendlini (njengokuphakamisa amathoyizi akho)	0	2	4
7. Ngabe unakho ukulimala noma ubuhlungu (Kuphi?)	0	2	4
8. Ngabe uke uzizwe ukhathele kakhulu ukuthi ungadlala	0	2	4

***Khumbula, ngitshele ukuthi kube yinkinga kangakanani lokhu kuwe emasontweni ambalwa edlule.***

<b>Imizwa Yakho (izinkinga ...)</b>	<b>Akuyis o Nhlobo</b>	<b>Ngezinye izikhathi</b>	<b>kakhulu</b>
1. Uzizwa wethukile	0	2	4
2. Uzizwa uphatheke kabi	0	2	4
3. Uzizwa uthukuthele	0	2	4
4. Unenkinga yokulala	0	2	4
5. Uyakhathazeka ngokuthi yini ezokwenzeka kuwe	0	2	4

<b>Abangane Nalabo Ofunda Nabo (izinkinga ...)</b>	<b>Akuyis o Nhlobo</b>	<b>Ngezinye izikhathi</b>	<b>kakhulu</b>
1. Kunzima kuwe ukuzwana nezinye izingane	0	2	4
2. Ziyasho ezinye izingane ukuthi azifuni ukudlala nawe	0	2	4
3. Ziyakusukela ezinye izingane	0	2	4
4. Ezinye izingane ziyakwazi ukwenza izinto wena ongakwazi ukuzenza	0	2	4
5. Kunzima kuwe ukuba sezingeni elifanele lapho udlala nezinye izingane	0	2	4

<b>Ukusebenza Esikoleni (izinkinga ...)</b>	<b>Akuyis o Nhlobo</b>	<b>Ngezinye izikhathi</b>	<b>kakhulu</b>
1. Kunzima kuwe ukulalela esikoleni	0	2	4
2. Uyazikhohlwa izinto	0	2	4
3. Kunzima kuwe ukuba sezingeni elifanele ngemisebenzi yasesikoleni	0	2	4
4. Uyaputha esikoleni ngenxa yokungazizwa kahle	0	2	4
5. Uyaputha esikoleni ngoba kufanele uye kwadokotela noma esibhedlela	0	2	4

# Kuyinkinga kangakanani lokhu kuwe?

Akusiyo Nhlobo



Ngezinye izikhathi



Kakhulu

